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FIFRA (Federal Insecticide, Fungicide and Rodenticide Act) Accelerated Reregistration: Phase 3 Technical Guidance

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The purpose of this guidance is to provide information to assist you in the preparation of your Phase 3 response for reregistration of your products. Phase 3 of reregistration is part of a five-phase process for the accelerated reregistration of pesticides established by Section 4 of the Federal Insecticide, Fungicide and Rodenticide Act (FIFRA). In Phase 3, registrants who seek reregistration but who are not eligible for a generic data exemption must determine which of their previously submitted scientific studies are adequate to support reregistration. This document contains guidance required by Section 4(e) of FIFRA concerning the adequacy of studies, how studies must be summarized and reformatted, and how to identify information on adverse effects.

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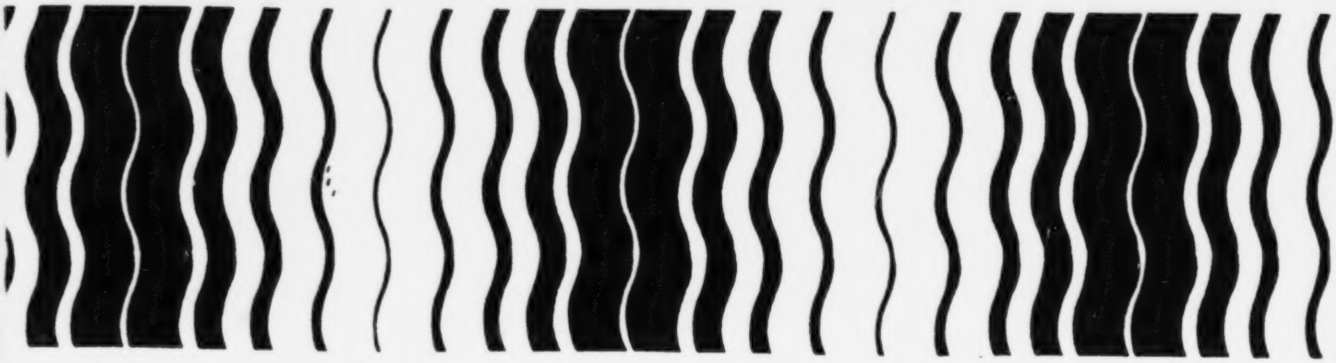

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OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

Dear Registrant:

Subject: FIFRA Accelerated Reregistration - Phase 3 Technical Guidance

The purpose of this guidance is to provide information to assist you in the preparation of your Phase 3 response for reregistration of your products. You must submit a Phase 3 response for every active ingredient for which you are responsible for providing generic data for reregistration. This guidance document will assist you in preparing Phase 3 responses for the studies that you consider adequate to support reregistration of your products.

Phase 3 of reregistration is part of a five-phase process for the accelerated reregistration of pesticides established by Section 4 of the Federal Insecticide, Fungicide and Rodenticide Act (FIFRA). Phase 1, now complete, involved the development and publication of Lists A, B, C, and D of pesticide active ingredients requiring reregistration. Phase 2, to be completed by January 24, 1990, is the initial response by all registrants indicating their desire to be reregistered, enumerating existing studies that fulfill data requirements, and obligating themselves to fill data gaps.

In Phase 3, registrants who seek reregistration but who are not eligible for a generic data exemption must determine which of their previously submitted scientific studies are adequate to support reregistration. To do so, they must apply certain criteria of data acceptability that the Agency has defined. In addition, they must summarize each study they wish to rely on for reregistration, reformat certain studies submitted before January 1, 1982, in accordance with Agency guidance, and identify information on adverse effects.

This document contains guidance required by Section 4(e) of FIFRA concerning the adequacy of studies, how studies must be summarized and reformatted, and how to identify information on adverse effects. It also contains guidance on how to determine whether to generate data on anticipated residues of pesticides on food and feed, and an overview of EPA's current guidance on toxicology and residue chemistry.

This guidance document contains all the information necessary to begin preparing your Phase 3 response. Supplementary guidance will be mailed to you containing specific information relevant to your company and your Phase 2 response after EPA has reviewed your Phase 2 response. This supplementary guidance will contain a form that you must use to summarize your Phase 3 response to EPA.

Phase 3 responses are due to the Agency no later than one year after publication of Lists B, C, and D in the FEDERAL REGISTER. Phase 3 responses for List B are due on May 25, 1990; Phase 3 responses for List C are due on July 24, 1990; and Phase 3 responses for List D are due on October 24, 1990. Failure to provide an adequate Phase 3 response in a timely manner may lead to cancellation of product registration without a hearing.

This guidance document and the instructions for your Phase 3 response has been approved by the Office of Management and Budget (OMB) and has been assigned OMB No. 2070-0106.

If, after reviewing this document, you do not understand the requirements for your Phase 3 response, call the Chemical Review Manager for your chemical in the Generic Chemical Support Branch at 1-800-552-8879 for further information. The Agency will assist you in every reasonable way.

Sincerely,

Douglas D. Campt

Douglas D. Campt, Director
Office of Pesticides Programs

Enclosure

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LIST OF ABBREVIATIONS AND ACRONYMS

ADI - Acceptable Daily Intake
AI - Active Ingredient
B.P. - Boiling Point
b.u.n. - blood urea nitrogen
CAS - Chemical Abstract Service
CFU - Colony Forming Units
cm - centimeters
CSPI - Center for Science in the Public Interest
DRES - Dietary Residue Evaluation System
DRG - Data Reporting Guidelines
EC25 - Effective Concentration 25
EC50 - Effective Concentration 50
EP - End-use Product
EPA - Environmental Protection Agency
FAO - Food and Agriculture Organization
FAT - Food Additive Tolerance
FDA - Food and Drug Administration
FFDCA - Federal Food, Drug and Cosmetic Act
FIFRA - Federal Insecticide, Fungicide and Rodenticide Act
GLP - Good Laboratory Practices
GPA - Gallons per Acre
HPLC - High Performance Liquid Chromatography
IUPAC - International Union of Pure and Applied Chemistry
kg - kilogram
L - liters
LC50 - Lethal Concentration 50
LD50 - Lethal Dose 50
LOD - Limit of Detection
LSC - Liquid Scintillation Count
MATC - Maximum Allowable Toxicant Concentration
meq - milliequivalents
mg - milligrams
mL - milliliters
mm - millimeters
MP - Manufacturing Use Product
MPCA - Microbial Pest Control Agent
MRID - Master Record Identification Number
MS - Mass Spectroscopy
MTD - Maximum Tolerated Dose

LIST OF ABBREVIATIONS AND ACRONYMS, continued

NFPA - National Food Processors Association
NOAEL - No Observed Adverse Effect Level
NOEL - No Observed Effect Level
NTIS - National Technical Information Service
o/oo - parts per thousand
OECD - Organization of Economic Cooperation and Development
OMB - Office of Management and Budget
OPP - Office of Pesticide Programs
PAG - Pesticide Assessment Guidelines
PAIRA - Pure Active Ingredient Radiolabelled
PFU - Plaque Forming Units
PHI - Preharvest Interval
ppm - parts per million
r.a.c. - raw agricultural commodity
SEP - Standard Evaluation Procedure
TAS - Tolerance Assessment System
TGAI - Technical Grade Active Ingredient
TLC - Thin Layer Chromatography
TRR - Total Radioactive Residue
μg - micrograms
ULV - Ultra Low Volume
USDA - United States Department of Agriculture

1. HOW TO USE THIS PACKAGE

1.1 What is the purpose of this package?

Use this package to help prepare your Phase 3 submission to the Environmental Protection Agency (EPA or the Agency). If you have completed, or will complete, Part B of the "Reregistration Phase 2 Response Worksheet" for a chemical on reregistration lists B, C, and D, EPA will be mailing you the "Phase 3 Chemical Response Worksheet" and the "Phase 3 Report and Worksheet on Product Status." These forms will be specific to your company and product(s). *Please read and follow the technical guidance in this package to evaluate existing studies, to summarize studies, and to reformat studies. Use the Phase 3 worksheets as a final summary of your response.*

1.2 What does this package contain?

The package contains the following guidance for reregistration, prepared by EPA as mandated by section 4(e) of the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA):

- How to determine if a study meets EPA's acceptance criteria (Chapter 2 and Appendix C)
- How to summarize studies (Chapter 2 and Appendix C)
- How to reformat studies (Chapter 3)
- How to identify information on unreasonable adverse effects (Chapter 4 and Appendix I).

EPA has also prepared additional guidance it believes will be useful for registrants reregistering their products:

- A new PR Notice (PR 89-3) describing the standard format for Phase 3 summaries and reformatted versions of studies previously submitted under FIFRA and certain provisions of the Federal Food, Drug, and Cosmetic Act (FFDCA) (Appendix B)
- How to determine if you should generate data on anticipated residues for pesticides used on food or feed (Chapter 5).
- Overviews of Technical Guidance for Subdivisions F and O (Appendices D and E)

1.3 How to use this package to organize your Phase 3 response

To develop your Phase 3 response for an active ingredient, you should review all the information you plan to use to support reregistration of pesticide products containing that chemical. First identify all previous communications to EPA concerning existing studies that may support reregistration.

A study is the report of a single scientific investigation, including all supporting analyses required for logical completeness. The communications associated with a single study should include all related documents, supplements, and supporting analyses previously submitted to EPA that are essential to the understanding of the scientific investigation. (See PR Notice 89-3 for additional discussion of what constitutes a study.) Registrants should identify all communications associated with a single scientific investigation that may support reregistration and consider them *as a single unit to be summarized and reformatted*, even if those communications were submitted at different times to the Agency.

Once you have identified the studies that may support reregistration, you should consider whether those studies are likely to be considered acceptable by EPA. EPA has provided acceptance criteria to help you assess whether a study is likely to be found acceptable by the Agency. These criteria are provided as *general guidance* on acceptability. EPA realizes that many studies may not meet all the acceptance criteria but may still be determined acceptable for reregistration.

If you find that a study satisfies EPA's acceptance criteria, or believe that it should be considered in reregistering your product even though it does not satisfy all of EPA's acceptance criteria, you must summarize that study in your Phase 3 response by following the guidance provided in this package. The guidance shows registrants how they may summarize and provide justification of studies that do not meet all of EPA's acceptance criteria. If, however, after reviewing the acceptance criteria, you decide not to rely on an existing study to fulfill a data requirement, you must conduct a new study or take alternative action to meet the data requirements for reregistration. The "Phase 3 Chemical Response Worksheet" will allow you to summarize for EPA your commitments to meet or to change the data requirements you previously indicated on your "Phase 2 Response Worksheet."

In summarizing each study, you must also determine whether it contains information on unreasonable adverse effects. Follow the guidance in Chapter 4 and Appendix I to determine the information that must be identified in a summary and use the "Phase 3 Chemical Response Worksheet," as explained in Chapter 4, to indicate which summaries contain such information. Chapter 4 also indicates how to identify information on unreasonable adverse effects if such information is not associated with a study being summarized in Phase 3.

After you have identified the studies you wish to summarize, you must reformat certain residue chemistry and toxicology studies conducted before 1982. Chapter 3 identifies which studies must be reformatted and explains how to reformat them.

This guidance package also contains a chapter on anticipated residues (pesticide residues in food at the time of consumption, as opposed to the tolerance, the *maximum* legal residue). Registrants are encouraged to conduct such studies early in the reregistration process so that more realistic dietary exposure assessments can be obtained for estimating dietary risks from pesticides. EPA will *require* anticipated residue studies in cases in which unacceptable risks are calculated based on tolerance level residues on food or based on tolerance level residues in conjunction with information on the percent of crop treated with a pesticide. Chapter 5 discusses the factors registrants should consider when designing monitoring studies and degradation studies (e.g., storage, cooking, peeling). If you decide to conduct a study on anticipated residues, indicate your intention on the "Phase 3 Chemical Response Worksheet."

1.4 When will you receive the "Phase 3 Chemical Response Worksheet" and the "Phase 3 Report and Worksheet on Product Status" for your active ingredients?

After EPA has received and processed your "Phase 2 Response Worksheet," the Agency will send you forms specially prepared for your active ingredients and products. You must complete the "Phase 3 Chemical Response Worksheet" and use it as a transmittal document that summarizes the information in your Phase 3 response.

1.5 How to obtain additional information on Phase 3 submissions.

For further information on the requirements of Phase 3 contact the Chemical Review Manager for the chemical in the Generic Chemical Support Branch at (800) 552-8879.

2. HOW TO SUMMARIZE STUDIES

The required elements for Phase 3 study summaries are listed in Appendix B (PR Notice 89-3), Part VIII. Table 1 lists information that must appear in the *Body of the Summary* for two categories of studies: (1) studies that were initiated after October 1984 *and* were approved by EPA, and (2) all other studies being relied on for reregistration. An abbreviated summary may be submitted for studies in category (1). A standard summary must be submitted for all other studies. Table 1 also indicates where additional guidance may be found for summarizing studies. The remainder of this chapter provides general guidance on topics relevant to study summaries and describes how to use the specific guidance given in Appendix C. The chapter also includes a definition of raw data. As described in Appendix B (PR Notice 89-3), registrants must certify access to raw data as part of each Phase 3 summary. Several sample Phase 3 summaries appear in Appendix A.

2.1 Acceptance Criteria

Appendix C lists, by guideline reference number, the criteria that generally distinguish an acceptable study from a study that cannot be used to support reregistration. EPA has provided these criteria so registrants can assess whether a study is likely to be found acceptable by the Agency. EPA realizes that research on pesticides is complex and does not intend the criteria to be used as an inflexible checklist. The Agency acknowledges that acceptable studies exist that do not meet all the acceptance criteria, and also that studies may be fundamentally flawed even though they seem to meet all the criteria. If you believe that a study that deviates from EPA's acceptance criteria should still be considered to support reregistration, you may summarize that study in your Phase 3 Response.

Appendix C lists two kinds of acceptance criteria: criteria that have been reviewed by EPA's Scientific Advisory Panel and have received public notice and comment; and supplemental criteria (marked with an asterisk) that identify additional factors the Agency believes are useful to consider when determining the adequacy of a study.

EPA requires the submission of acceptance criteria worksheets when registrants choose the abbreviated summary format for studies initiated after October 1984 that have been reviewed and approved by EPA. The submission of acceptance criteria worksheets is strongly recommended for all summaries. A standard summary must identify any acceptance criteria not met and explain why the study should nevertheless be considered irrespective of whether or not the acceptance criteria worksheet is included.

2.2 Traditional Laboratory Summary

If a study is eligible for the abbreviated summary format, registrants may include in their Phase 3 Response a traditional laboratory summary that includes, as a minimum: an identification of test materials and methods, a summary of the results of the study, and the date of test initiation and termination. Registrants may provide a legible photocopy of the summary of the initial study report if that summary includes the information listed above. Registrants summarizing residue chemistry studies are also asked to identify the tolerance petition numbers associated with those studies, if the studies have been used to support a tolerance.

TABLE 1. INFORMATION TO APPEAR IN THE BODY OF A STUDY SUMMARY.

ABBREVIATED SUMMARY - OPTIONAL FOR STUDIES INITIATED AFTER 1984 THAT HAVE BEEN APPROVED BY EPA

Item	Guidance
Completed acceptance criteria worksheet	Chapter 2.1 and Appendix C
Traditional laboratory summary	Chapter 2.2
Evidence that the study was reviewed by EPA and found acceptable	Chapter 2.3
Identification of information concerning unreasonable adverse effects	Chapter 4

STANDARD SUMMARY - REQUIRED FOR ALL OTHER STUDIES

Item	Guidance
Completed acceptance criteria worksheet (optional)	Chapter 2.1 and Appendix C
Identification of any acceptance criteria not met and an explanation of why the study should nevertheless be considered	Chapter 2.1
Identification of test material	Chapter 2.4
Items specific to individual guideline reference numbers	Chapter 2.5 and Appendix C
Identification of information concerning unreasonable adverse effects	Chapter 4

2.3 Evidence that the Summary was Reviewed by EPA and Found Acceptable

If a registrant finds that a study is eligible for the abbreviated summary format, the registrant must provide EPA with the supporting evidence that the study was reviewed by EPA and found acceptable. This information may include a copy of EPA's review of the study, a letter from a Product Manager stating that EPA has found the study acceptable, or other information that the registrant typically relies on to determine whether a study was found acceptable by EPA.

2.4 Identification of Test Material

The identification of the test material for all non-microbial pesticides should include:

- Chemical name [Chemical Abstract Service (CAS) name preferred], common name, and trade name. International Union of Pure and Applied Chemistry (IUPAC) designation is requested.
- CAS number of active ingredient
- Chemical structure of active ingredient
- Percent active ingredient
- Identity and composition of impurities

Unless otherwise indicated in Appendix C, EPA expects registrants to have used the technical grade of the active ingredient in product chemistry studies and other studies.

If the test substance is a microbial, the identification must include:

- Scientific name and, to the extent possible, serotype and strain or other appropriate designated type, and, to the extent possible, a qualitative and quantitative determination of composition (including names and quantities of known contaminants and impurities, within technically feasible limits). The determination shall also include quantities of unknown materials, if any, to account for 100% of the sample;
- Manufacturer and lot number of the test substance, and relevant properties of the substance tested, (i.e., physical state, pH, stability, and purity); and
- Identification and composition of any vehicles or other materials (e.g., diluents, suspending agents, emulsifiers, virulence enhancers) used in administering the test.

2.5 Guidance Specific to Individual Studies

Appendix C also identifies by individual Guideline Reference Number the specific information that should be included in a summary. This guidance highlights the information of greatest importance to EPA's review and is designed to expedite both the registrants' preparation of study summaries and EPA's review.

EPA recognizes that even though a study may meet the acceptance criteria for a guideline requirement, it may not necessarily contain all the information listed in the guidance for summarizing studies. In that case, the summary must contain all the information available that addresses the specific summary guidance provided.

If the summary guidance for a specific study calls for a "summary of conclusions," limit your summary to one or two sentences that state the conclusions. For example, if you are summarizing a hydrolysis study, a sentence or two indicating whether the chemical is stable in water or breaks down rapidly is all that is needed. In contrast, the discussion of results should provide additional information regarding the results. This should include such information as a discussion of any problems that occurred during the study and deviation from protocols.

EPA has specified in Appendix C (for example, Guideline Reference No. 171-3) when summaries are not required. If no summary guidance is provided for a specific guideline number and no specific exemption or exclusion is identified, you should include in the summary an identification of test materials and methods, results, discussion of results, conclusions, and the date of test initiation and termination.

2.6 Raw Data

FIFRA states that each registrant seeking reregistration must submit "a certification that the registrant or the EPA Administrator possesses or has access to the raw data used in or generated by" the study that is being summarized. A standard format for this certification appears in Appendix B (PR Notice 89-3). A certification statement must be included in each study summary.

For toxicology studies initiated or conducted after December 29, 1983, and for studies in chemistry, environmental fate, or ecological effects, the definition of "raw data" provided by the Good Laboratory Practice (GLP) Standard serves as a guide (40 CFR 160.3). The GLP defines "raw data" as

> *any laboratory worksheets, records, memoranda, notes, or exact copies thereof, that are the results of original observations and activities of a study and are necessary for the reconstruction and evaluation of the report of that study. In the event that exact transcripts of raw data have been prepared (e.g., tapes which have been transcribed verbatim, dated, and verified accurate by signature) the exact copy or exact transcript may be substituted for the original source as raw data. "Raw data" may include photographs, microfilm, or microfiche copies, computer printouts, magnetic media, including dictated observations, and recorded data from automated instruments.*

EPA has described in Appendix H the specific types of information it considers to be "raw data" for studies in different subdivisions. EPA will also consider the raw data requirement satisfied if the study has been audited by EPA and the audit found that all raw data needed for reconstructing the study were present.

3. REFORMATTING STUDIES

3.1 What data must be reformatted?

FIFRA requires registrants who submitted studies concerning chronic dosing, oncogenicity, reproductive effects, mutagenicity, acute and subchronic neurotoxicity, teratogenicity or residue chemistry before January 1, 1982, and who are relying on those studies to support reregistration to reformat the data from each of those studies. In addition, if the toxicology studies listed above are not required by regulations issued under section 3 for an active ingredient, FIFRA states that registrants must reformat the reports of acute and subchronic dosing they submitted before January 1, 1982.

EPA has decided that two categories of studies identified by FIFRA do not require special reformatting: (1) oncogenicity studies in the mouse that have been through the Office of Pesticide Program's peer review and have been classified by EPA, and (2) acute toxicity studies. For those categories of studies, the summary information registrants will supply in Phase 3 will provide sufficient reformatted information for EPA's review.

3.2 How must these data be reformatted?

Registrants must:

1. reformat all data developed for a single toxicology study or for a single residue chemistry study in *one* report. If any report of a study was submitted before January 1, 1982, *all* data for that study, even if submitted after 1982 must be included in the reformatted report. PR Notice 89-3 in Appendix B provides a definition of a study;

2. follow the standard guidance in PR Notice 89-3 concerning format standards; and

3. follow the special instructions for data reporting developed by EPA for each guideline. This guidance is available, on request, from the National Technical Information Service (NTIS).

3.3 What information is available as guidance from NTIS on reformatting data?

EPA has made available through NTIS all the guidance relevant to reporting the data from toxicology and residue chemistry studies for chemical pesticides. EPA has also developed an overview of the technical guidance relevant to toxicology and residue chemistry studies for chemical pesticides. This guidance appears in Appendices D and E. It explains the relationship between EPA's data reporting guidelines and the other technical guidance documents available from NTIS. This guidance is entitled "Overview of Subdivision F - Hazard Evaluation; Humans and Domestic Animals" and "Overview of Subdivision O - Residue Chemistry."

Each overview lists EPA publications pertaining to the relevant subdivision and identifies how they are related to specific guideline reference numbers. The overview also identifies EPA's most current guidance for generating and reporting data, clarifies some apparent inconsistencies between the Pesticide Assessment Guidelines, Data Reporting Guidelines, and Standard Evaluation Procedures, and indicates future directions that the Agency is considering.

Registrants seeking to reregister microbial pesticide products should consult "Pesticide Assessment Guidelines, Subdivision M; Part A, Microbial Pest Control Agents" (NTIS Number PB89-211676) for guidance on reformatting toxicology and residue chemistry studies for such pesticides. Registrants who wish to reregister biochemical pesticide products should consult "Pesticide Assessment Guidelines, Subdivision M; Biorational Pesticides" (NTIS number PB83-153965) for the most current guidance on data submission.

3.4 Is any additional information needed for reformatting specific studies, other than guidance available from NTIS?

The documents available from NTIS provide all the guidance needed for reformatting toxicology studies. For residue chemistry, however, specific data reporting guidelines are only available for the major types of residue chemistry studies.

3.5 How should registrants reformat data for the residue chemistry studies for which specific data reporting guidelines are not available?

EPA suggests that registrants use the guidance available for reporting the study "Magnitude of the Residue: Crop Field Trials" [Guideline Reference Number: 171-4(k)] for reporting results from studies of the "Magnitude of the Residue" for potable water, fish, irrigated crops, and food handling [Guideline Reference Numbers: 171-4(f); 171-4(g); 171-4(h); and 171-4(j)]. Registrants should use the guidance available from NTIS, and interpret the water, fish, irrigated crops and food being tested as the "Test Commodity." EPA suggests that registrants use their judgement to decide when test parameters described for the major study are not applicable (e.g., to decide that identifying soil characteristics may not be relevant if the study concerns food handling) or need to be interpreted in a different context (e.g., to decide that a description of a field trial design would not be relevant to the context of a study of a food handling use, but that a description of the restaurant where the food handling occurs would be).

The other residue chemistry data requirement for which no published data reporting guidance exists is "Reduction of the Residue" (Guideline Reference Number: 171-5). The Agency suggests the use of guidance developed for "Processed Food/Feed Study" [Guideline Reference Number: 171-4(l)] for reporting data for this study. Where the guidance calls for information on "Test Procedures," EPA suggests that the submitter describe how the commodity was washed, cooked or stored, prior to residue analysis.

4. IDENTIFYING INFORMATION REGARDING UNREASONABLE ADVERSE EFFECTS

As part of your Phase 3 submission you must identify information relevant to EPA's determination of whether a pesticide poses unreasonable adverse effects. (This requirement is stated in FIFRA Section 4(e), which refers to information that must be submitted under FIFRA Section 6(a)(2).) Note that the information need not, by itself, demonstrate unreasonable adverse effects. The information need only be relevant to EPA's determination of whether any adverse effects are reasonable or not.

This chapter has two parts. Section 4.1 describes how to determine which "pieces" of information should be identified. Section 4.2 describes how to identify the information in your Phase 3 submission.

4.1 What Information Must be Identified?

The criteria described in Appendix I must be used to determine which pieces of information must be identified. A "piece" of information is any study, incident, or other information pertaining to the active ingredient which is known to the registrant, whether or not the information has already been submitted to EPA, and whether or not the registrant possesses documents related to the information.

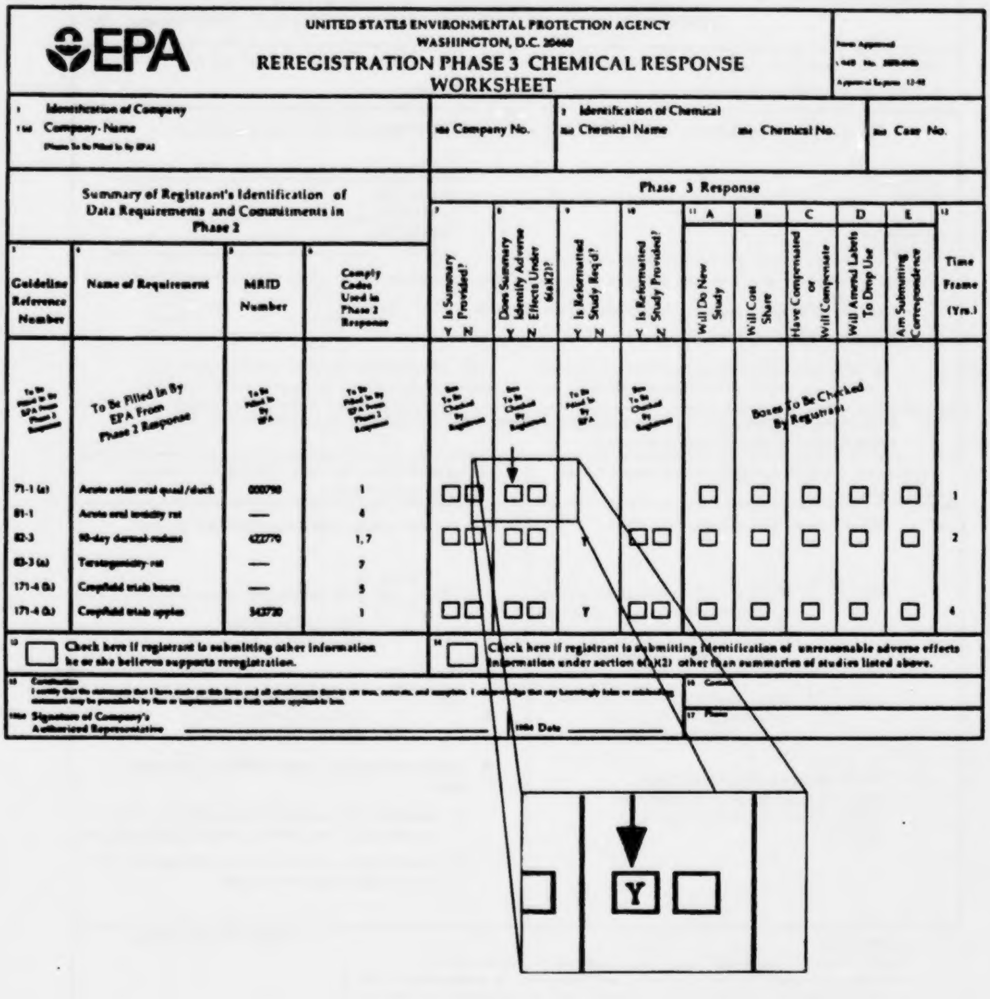
Make a list of all pieces of information. For each piece of information on the list use the guidance in Appendix I to determine whether the information would be submissable under FIFRA Section 6(a)(2), assuming that the information has not yet been submitted, but all other pieces of information on your list have been submitted to EPA.

4.2 How to Identify Information in Your Phase 3 Submission

If any piece of information would be submissable as described above, it must be identified in one of two ways:

(1). If the piece of information is part of a study that you are using in support of reregistration, identify the information in the study summary and check "Y" in column 8 of the Phase 3 Chemical Response Worksheet, which you will receive later in a separate mailing. An example showing how to use the worksheet to identify unreasonable adverse effects appears in Figure 1.

(2). If the piece of information is not part of a study that you are using in support of reregistration, complete the form shown in Figure 2. Two copies of this form ("Phase 3 Identification of Unreasonable Adverse Effects Information Not Indicated on the Phase 3 Worksheet") are provided in Appendix G for your use.



UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460
REREGISTRATION PHASE 3 CHEMICAL RESPONSE WORKSHEET

Form Approved
OMB No. [illegible]
Approval Expires [illegible]

1 Identification of Company
1a Company Name (Name To Be Filled In by EPA)
1b Company No.
2 Identification of Chemical
2a Chemical Name
2b Chemical No.
2c Case No.

Summary of Registrant's Identification of Data Requirements and Commitments in Phase 2

Phase 3 Response

3 Guideline Reference Number	4 Name of Requirement	5 MRID Number	6 Comply Codes Used in Phase 2 Response	7 Is Summary Provided? Y N	8 Does Summary Identify Adverse Effects Under 6(a)(2)? Y N	9 Is Reformatted Study Req'd? Y N	10 Is Reformatted Study Provided? Y N	11 A Will Do New Study	B Will Cost Share	C Have Compensated or Will Compensate	D Will Amend Labels To Drop Use	E Am Submitting Correspondence	12 Time Frame (Yrs.)
To Be Filled In By EPA From Phase 2 Response	To Be Filled In By EPA From Phase 2 Response	To Be Filled In By EPA	To Be Filled In By EPA From Phase 2 Response	Box To Be Checked By Registrant	Box To Be Checked By Registrant	To Be Filled In By EPA	Box To Be Checked By Registrant	Boxes To Be Checked By Registrant					
71-1 (a)	Acute avian oral quail/duck	000790	1	☐ ☐	☐ ☐			☐	☐	☐	☐	☐	1
81-1	Acute oral toxicity rat	—	4										
82-3	90-day dermal-rodent	422770	1, 7	☐ ☐	☐ ☐	Y	☐ ☐	☐	☐	☐	☐	☐	2
83-3 (a)	Teratogenicity-rat	—	7										
171-4 (b)	Cropfield trials beans	—	5										
171-4 (b)	Cropfield trials apples	343730	1	☐ ☐	☐ ☐	Y	☐ ☐	☐	☐	☐	☐	☐	4

13 ☐ Check here if registrant is submitting other information he or she believes supports reregistration.

14 ☐ Check here if registrant is submitting identification of unreasonable adverse effects information under section 6(a)(2) other than summaries of studies listed above.

15 Certification
[illegible]

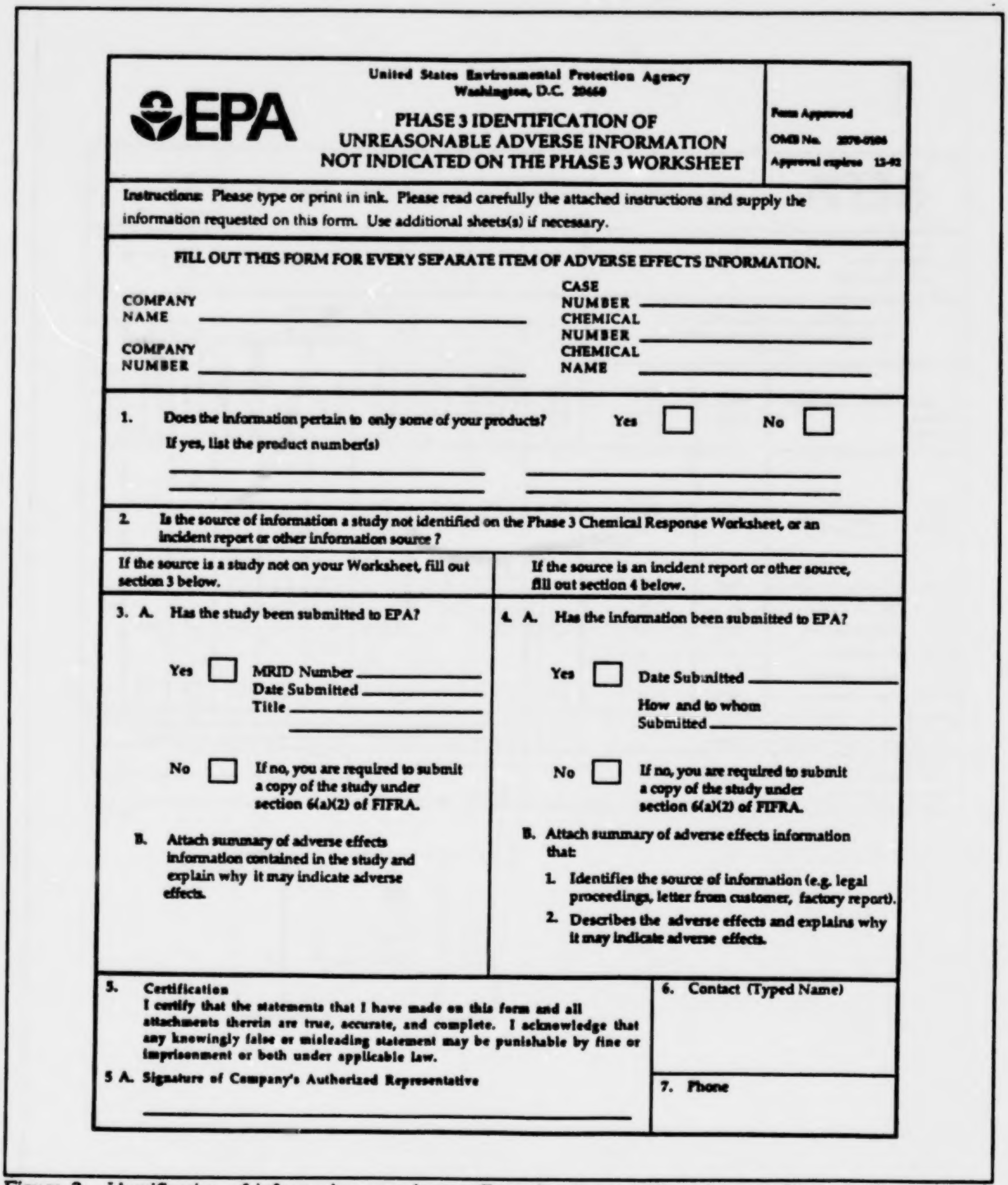
15a Signature of Company's Authorized Representative ______________

15b Date ______________

16 Contact

17 Phone

Figure 1. *Identifying unreasonable adverse effects on the Phase 3 Chemical Response Worksheet.*



EPA

United States Environmental Protection Agency
Washington, D.C. 20460

PHASE 3 IDENTIFICATION OF UNREASONABLE ADVERSE INFORMATION NOT INDICATED ON THE PHASE 3 WORKSHEET

Form Approved
OMB No. 2070-0106
Approval expires 12-92

Instructions: Please type or print in ink. Please read carefully the attached instructions and supply the information requested on this form. Use additional sheets(s) if necessary.

FILL OUT THIS FORM FOR EVERY SEPARATE ITEM OF ADVERSE EFFECTS INFORMATION.

COMPANY NAME ______________________
COMPANY NUMBER ______________________
CASE NUMBER ______________________
CHEMICAL NUMBER ______________________
CHEMICAL NAME ______________________

1. Does the information pertain to only some of your products? Yes ☐ No ☐
If yes, list the product number(s)
______________________ ______________________
______________________ ______________________

2. Is the source of information a study not identified on the Phase 3 Chemical Response Worksheet, or an incident report or other information source?

If the source is a study not on your Worksheet, fill out section 3 below.

3. A. Has the study been submitted to EPA?

Yes ☐ MRID Number ______________
Date Submitted ______________
Title ______________
____

No ☐ If no, you are required to submit a copy of the study under section 6(a)(2) of FIFRA.

B. Attach summary of adverse effects information contained in the study and explain why it may indicate adverse effects.

If the source is an incident report or other source, fill out section 4 below.

4. A. Has the information been submitted to EPA?

Yes ☐ Date Submitted ______________
How and to whom Submitted ______________

No ☐ If no, you are required to submit a copy of the study under section 6(a)(2) of FIFRA.

B. Attach summary of adverse effects information that:

1. Identifies the source of information (e.g. legal proceedings, letter from customer, factory report).
2. Describes the adverse effects and explains why it may indicate adverse effects.

5. Certification
I certify that the statements that I have made on this form and all attachments therein are true, accurate, and complete. I acknowledge that any knowingly false or misleading statement may be punishable by fine or imprisonment or both under applicable law.

5 A. Signature of Company's Authorized Representative
____

6. Contact (Typed Name)

7. Phone

Figure 2. *Identification of information on adverse effects that is not indicated on the Phase 3 Chemical Response Worksheet. Copies of this form are provided in Appendix G for your use.*

5. GENERATING DATA ON ANTICIPATED RESIDUES

During the reregistration process mandated by FIFRA, EPA will assess human health risks from pesticide residues in food. EPA strongly encourages registrants to submit data on anticipated residues to improve the assessment. If data are not provided voluntarily, EPA will base the assessment on less realistic methods such as tolerances or tolerances combined with data on percent crop treated. These estimates will be based on currently available field trial and processing data. If the risks calculated by EPA are unacceptable, EPA will require anticipated residue data to be provided. Registrants would then have to provide this data or propose to modify the use of their chemical by changing, for example, the rate, number or type of applications, or by deleting uses.

Two types of data are requested -- degradation studies and monitoring data. Each type is discussed in more detail below. Additional guidance will be available in mid-1990. Generation of these types of data, which are not routinely required by EPA, would be beneficial to both the Agency and the registrant since it would permit more realistic estimates of exposure that are likely to be lower than estimates based on currently available data.

The human health risk from exposure to pesticide residues in food is a function of the toxicity of the pesticide, the amount of food consumed, and the level of residues in the food. EPA has developed a computer-based system called the Dietary Risk Evaluation System (DRES), formerly called the Tolerance Assessment System (TAS), to integrate this information. DRES estimates dietary exposure in terms of quantity of pesticide consumed per unit body weight per day and compares it to a previously determined Acceptable Daily Intake (ADI) or similar toxicological threshold. Consumption patterns are derived from a 1977-78 U. S. Department of Agriculture survey involving 3-day dietary records for 30,770 individuals and 3,734 food items (food forms). DRES can handle separate residue estimates for multiple food forms of a single commodity. For example, food forms for apples include fresh apples, cooked apple products and apple juice. Dietary exposure can be estimated for the entire U.S. population and for 22 subgroups, determined by such factors as age, sex, ethnic background, and geographic region.

When alternative data are not available, EPA enters tolerance level residues into DRES. This approach will tend to overestimate exposure because a tolerance level is the maximum allowable residue on a commodity and should not commonly be reached or exceeded from proper product use. DRES is also capable of using "anticipated residues" which are more realistic estimates of residues in food at time of consumption and consequently lead to more realistic estimates of exposure and risk.

The method used to quantify the anticipated residue depends on the toxic effect of the pesticide. For acute effects, the most appropriate quantity might be the maximum amount of pesticide residue likely to be consumed in a given period (e.g., meal, day, week, etc). For chronic effects, the average residue level over a longer period of time might be more appropriate.

5.1 Degradation Studies (Storage, Transport, Processing, Cooking, Washing, Peeling)

Degradation refers to the change in the amount and composition of the total residue from harvest to the point of consumption. For pesticides applied after harvest, degradation describes the change from pesticide application to consumption. Two general degradation scenarios are possible. The pesticide may degrade to form less toxic products, or the pesticide may degrade to form more toxic chemical compounds.

The Agency does not recommend a specific protocol, but urges the registrant to submit a protocol for Agency review before initiating a degradation study. Degradation studies for representative commodities within a commodity group may be sufficient if commercial and home practices are similar for the different commodities. EPA is working with the National Food Processors Association (NFPA) to develop protocols for processing studies for some commodities. These are available from NFPA or from the Dietary Exposure Branch of EPA.

After harvest, commodities can be stored (sometimes for extended periods of time), transported, commercially processed, waxed, washed, peeled, cooked, and treated in other commodity-specific ways (e.g. removal of the outer leaves from lettuce). A typical degradation study should take a large treated sample through all the processes from harvest to consumption, and should simulate typical commercial and home practices as closely as possible. Subsamples should be removed at each important point for residue determination in the edible portion of the commodity. In all cases, but particularly when degradation products are more toxic than the parent, application rates should be chosen which are close to the maximum registered rates so that metabolite ratios likely to result from typical applications can be determined. Residues in the raw commodities at the beginning of the study should be well above the limit of detection (LOD) of the analytical method so that a decline in residues can be measured. Analytical methods must have sufficiently low LODs so that, when calculated at the LOD, the risk from the measured residues can be determined to be acceptable.

Time and temperature considerations are important when examining storage, transportation, commercial processing, and cooking. Humidity may be important when examining storage and transportation. The point at which wax is applied to some commodities must be considered (e.g. citrus, cucumbers.) The typical way(s) commodities are washed, peeled and cooked (e.g. boiled, fried, roasted, etc.) are important considerations. Other processes may also be important for specific commodities (e.g. shelling nuts, removal of the outer leaves from lettuce and cabbage, removal of the thick part of the stem from broccoli and asparagus.)

5.2 Monitoring Data

A monitoring program (or survey) is a study in which samples of agricultural commodities/foods are obtained (usually at the retail level) and analyzed for pesticide residues. Residue levels determined in this way are likely to be more realistic estimates of dietary residues than tolerance levels. Sampling locations and numbers of samples obtained are chosen so that the residue levels measured are representative of residue levels found nationally in a specific commodity and satisfy pre-determined requirements of accuracy and precision.

EPA does not recommend any specific protocol, but urges registrants to submit the protocol for Agency review before initiating a study. Factors to be considered when preparing a protocol include which food forms to monitor and the point in the life of the commodity to obtain the samples, the required accuracy and precision of the results (which influences the number of samples required), the toxicological effect, and available analytical methodology. The following must be addressed:

- food forms to be analyzed (for guidance see "*Tolerance Assessment System, Food-Form Codes*", 10/84, USEPA/OPP)

- movement of the commodity in commerce (including storage times and conditions)
- the time of year or season in which the pesticide is applied (data should be obtained at various times or seasons throughout the year)
- the variability in growing conditions or agricultural practices for a commodity
- the percent of livestock treated
- the percent of crop treated and specific geographical areas likely to be treated based on usage data or on the geographical range of the pest being controlled
- the percentage each specific crop contributes to the total dietary exposure to a pesticide (in most cases it may be appropriate to generate data for representative commodities for crop groupings as defined in 40 CFR 180.34(f)(9))
- whether normal use of the pesticide may have temporarily declined due to adverse publicity (monitoring data may not be acceptable in this situation) or due to declining pest pressure
- the performance of the analytical method (if residues at the limit of detection of the analytical method are of toxicological concern, an alternative method may be necessary)
- the appropriateness of compositing samples (taking into account toxic effects and expected variability of residue levels) to reduce the total number of samples required
- commodities likely to contain detectable residues as determined by field trial data
- food forms consumed by population subgroups determined to be primarily at risk
- the active ingredient
- the availability of livestock feeding studies from which residues in animal products might be derived from residues measured in treated animal feeds
- the availability of processing data from which residues in processed commodities can be derived from residues measured in the raw commodity

APPENDIX A: SAMPLE SUMMARIES

SAMPLE SUMMARY FOR ECOLOGICAL EFFECTS STUDIES

Phase 3 Summary of MRID 111111;
Chemical A - Fish Early Life Cycle - Rainbow Trout: Project 99333

Guideline Reference:

72-4 Fish Early Life Stage Test - Rainbow Trout

Summary Prepared By:

A. Researcher
November 8, 1980

Original Study Prepared By:

Field Research, Inc.
Cincinnati, Ohio

Statement of No Data Confidentiality Claims

No claim of confidentiality is made for any information contained in this study on the basis of its falling within the scope of FIFRA section 10(d)(1)(A), (B), or (C).

Company:________________________________ (Typed Name)

Company Agent:________________________________ (Typed Name)

Title:________________________________

Signature:________________________________ Date:______________

Good Laboratory Practice Statement

This study meets the requirement for 40 CFR Part 160

Submitter of study:______________________________ (Signature)

Sponsor:______________________________ (Signature)

Study Director:______________________________ (Signature)

Certification of Availability of Raw Data

I hereby certify that the submitter possesses or has access to the raw data used in or generated by the study summarized in this document.

Submitter's Representative:

Signature/Date:____

Typed Name:____

Title:____________________________

Certification of Accuracy of Summary and Adequacy of the Study

I certify, in compliance with FIFRA section 4(e)(1)(B), that this summary accurately represents the data presented in the report(s) of this study cited by MRID. Although this study does not fully satisfy the requirements of the OPP Guideline it addresses, it should nonetheless be accepted in satisfaction of this Guideline requirement. The specific deficiencies of the study and the rationale for its acceptance in spite of those deficiencies are individually identified and discussed within this summary.

Submitter's Representative:

Signature/Date:____

Typed Name:____

Title:____________________________

SAMPLE SUMMARY FOR ECOLOGICAL EFFECTS STUDIES

Subdivision E
Guideline Ref. No. 72-4
December 24, 1989

72-4 Early Life Stages Test

ACCEPTANCE CRITERIA

Does your study meet the following acceptance criteria?

GENERAL INFORMATION

1. Y Date of test initiation and termination reported

MATERIALS/METHODS

2. Preparation of test solution (control/treatment) described
    - Y Any vehicle used to dissolve test material
    - Y If used, amount of vehicle added to control
    - Y Method used to get test material into solution was described
    - Y Water source
    - Y Water solubility of test material reported in ppm
    - •Y Total amount of test material used
    - •Y Temperature of water reported
    - •____ Salinity (o/oo), if estuarine species is tested

3. Test fish
    - Y One of the following organisms was tested: brook trout, rainbow trout, coho salmon, chinook, bluegill, brown trout, lake trout, northern pike, fathead minnow, channel catfish, sheepshead minnow, silverside
    - •Y History of test organisms described (strain, diseases and treatment)
    - •Y Health described (sickness; injuries; abnormalities; name of medication, if used; pretest diet, number of days brood fish were quarantined)

4. Size/age/physical condition
    - •Y Age of unfertilized eggs and milt at the beginning of test
    - •____ Procedures used to strip eggs and milt described
    - •Y Procedures used in storage and handling of eggs described
    - Y Fertilization process described

5.• Y Source/acclimation described -
Complete name and address of test fish supplier, source of food and dilution water, size of test container in milliliters (mL), temperature, pH, dissolved oxygen, name of equipment used to measure water quality, feeding schedule, holding, acclimation period, test organisms are from same source, number of days held, salinity (o/oo)

Criteria marked with a • are supplemental and may not be required for every study.

6. Composition and size of test vessels described

Y Material type
Y Volume in liters (L) or size in centimeters (cm)
Y Depth of test solution in cm or volume of dilution water (L)

7. Test system described

Y Source of dilution water
Y If flow-through, system and flow rate/day described
Y Procedures used to prepare toxicant stock solution
Y Criteria used to determine effects

8. Test design followed

Y Method used in assigning test organisms to test and control groups and number of replicates used
Y Number of eggs per dose level and control group (80)
*Y Name of protocol followed during this test
Y Loading (weight per unit volume of water)
Y 5 treatments and 1 control used
Y Length of exposure period
Y Type of control (positive, negative, or solvent control)
Y Temperature
Y pH
*Y Lighting (time in hours and intensity - footcandles)
Y Dissolved oxygen
Y Water hardness
*Y Alkalinity
*Y Conductivity (umhos/cm)
*Y Range finding test results (concentrations and mortality) if conducted
*Y Water: physical characteristic at the end of test - water depth and volume
Y Period food was withheld prior to termination
Y Method used to keep eggs clean described

DISCUSSION AND RESULTS

9. N **MATC value reported in ppm. Raw data provided.**

10. Y **Any precipitation and solubility problems described.**

11. Y **Statistical method referenced.**

12. Y **Discussion of concentration(s) producing intoxication provided.**
✓ Water: physical characteristic at the end of test - temperature, pH, and dissolved oxygen
✓ Concentration analysis (if flow through)

Criteria marked with a * are supplemental and may not be required for every study.

13. Y Signs of intoxication noted.
    - Y Number of embryos hatched per replicate reported
    - Y Time to hatch per replicate reported
    - Y Mortality of embryos, larvae, and juveniles per replicate reported
    - Y Time to swim-up per replicate reported
    - Y Measurements of growth-weight and length per replicate reported
    - Y Fish physiology, locomotion, behavior and pathology reported
    - Y When larvae fish released from the retaining cup, % complete or hours elapsed identified

14.* N No-observed-effect level, if determined.

15. The relationship between the results of the study and the test chemical described, including
    - Y Obvious problems that occurred during the study as well as the effect, if any, these problems had on the outcome of the study
    - ___ Rationale for minor deviations from the protocol

16.* Y Graphs, printouts and other calculations are attached to report

Criteria marked with a * are supplemental and may not be required for every study.

72-4 Fish Early Life Stage Test

Identification of Test Substance

Chemical A Technical; Batch No. 13-10-10-32; 93% active ingredient; a tan powder.

General Information

1. **Conclusions:**
The MATC of Chemical A Technical for rainbow trout (Salmo gairdneri) was < 0.062 mg AI/L based on mean measured concentrations.
Test initiation: 2/14/87 Test termination: 5/13/87

Materials/Methods

2. **Description of test solution (control/treatment) preparation, including:**
    a. Maximum solubility of 0.343 mg Chemical A/L was achieved after mixing for 48h in 0.05% acetone. Solubility of Chemical A in water (20° C) is 0.35 ppm.

3. **Description of test species**
    a. Rainbow trout (Salmo gairdneri)

4. **Description of source/acclimation, including:**
    a. Test fish were obtained from the Mt. Lassen trout farm, Red Bluffs, California.

    b. Sperm and eggs were received and fertilized at 8° C and gradually over 1 hour acclimated to test temperature (12° C).

5. **Description and size of test vessels**
Each glass aquarium measured 25 x 16 am with a water depth of 24 cm, yielding an approximate 9.6-liter replicate-chamber volume. The rainbow trout eggs were incubated in cups suspended in the treatment and control water. These egg incubation cups were made from 7-cm diameter tubing with stainless steel screening (16 mesh) fused to the bottom.

6. **Description of test system**
   a. Dilution water was aerated well water.

   b. The diluter delivered an average rate of approximately 63 mL/minute/replicate of test solution or control water to the test vessels which was sufficient to replace a replicate volume 9.4 times in a 24-hour period.

   c. The following parameters were studied: embryo viability, survival of organisms at hatch, larval survival, and growth. Growth, as determined by standard length of the fry, was determined by the photographic method of McKim and Benoit (1975) on study day 49. At test termination, study day 74 (60 days post-hatch), all surviving fish were measured for standard length and wet weight.

7. **Description of test design**
   a. A control, solvent control, and five nominal Chemical A Technical concentrations of 0.06, 0.12, 0.25, 0.50, and 1.0 mg/L based on active ingredient were tested. The solvent control solution contained the maximum amount of DMF present in any test concentration (0.014 mL/L). Thirty rainbow trout eggs were randomly introduced into each replicate chamber (60 eggs per concentration).

   b. The test chambers were immersed in a temperature controlled water bath held at 12 ± 2°C. During the testing period, the rainbow trout fry were on a 16-hour daylight photoperiod with the eggs shielded from excess U.V. light exposure. The light intensity was 158 ± 25 foot-candles at the water surface.

   c. The well water characterized as having a pH of 7.8 - 8.3.

   d. When hatching commenced, the number of eggs hatched in each incubation cup was recorded daily until hatching was completed. The 60-day post-hatch growth period began when hatching was greater than 95 percent (Day 14). On study-day 27 (13 days post-hatch), the rainbow trout sac fry were removed from the duplicate egg incubation cups and separated into 4 replicate growth chanbers per concentration. Survival and fry growth data were collected on Days 35 and 60 post-hatch. Feeding began on Day 27 (13 days post-hatch). The fry were fed brine shrimp nauplii three times each day. Commercial fish food was added to the diet as the fish became larger.

8. **Discussion and Results**

a. One-way analysis of variance (ANOVA) calculations were used to determine if significant differences existed between the control and treatment levels. If treatment effects were indicated by a significant F-test of the mean square ratios, Tukev's HSD multiple means comparison test was used to determine which exposure levels differed from the control values.

b. The mean measured concentrations of Chemical A Technical were 0.062, 0.097, 0.20, 0.41, and 0.84 mg AI/L. The mean measured concentrations ranged from 80 to 103% of the nominal test concentrations.

c. Based on the length and weight data from this 60-day post-hatch rainbow trout (Salmo gairdneri) early life state study, the Maximum Acceptable Toxicant Concentration (MATC) of Chemical A Technical was estimated to be < 0.062 mg AI/L, the lowest concentration tested.

d. Morphological and behavior abnormalities such as curved spine, fish resting on the bottom of the test chamber, loss of equilibrium, light discoloration, quiescence, enlarged yolk sac, and fishing swimming vertically in the test chamber were scattered throughout the controls and the three lowest test levels in a small percentage of the fish. By Day 50 (36 days post-hatch), most of these effects had either disappeared or the affected fish had died. Quiescence and fish resting on the bottom of the test chamber persisted in a few fish in the 0.20 mg AI/L concentration until just before test termination.

Results for the effect of Chemical A Technical on length of rainbow trout are shown in Table 1 (attached). The single surviving fish in the 0.41 mg AI/L concentration was not included in the 35-day post-hatch length analysis since a group that contains only one fish cannot be compared with other groups each containing several fish in an analysis of variance. The 0.20 mg AI/L concentration fish were the only test fish that showed a significant reduction in length when compared to the control at 35-days post-hatch. By 60-days post-hatch, the fish in the lowest three test concentrations all showed a significant ($P < 0.05$) length reduction when compared to the control.

Results for the effect of Chemical A Technical on wet weight of rainbow trout are shown in Table 1 (attached). Growth of the trout fry, as measured by wet weight after 60 days of exposure to Chemical A Technical, was significantly reduced in the lowest three test concentrations.

9. **Discussion relating results of study to test chemical**

a. Based on growth (weight and length), the Maximum Acceptable Toxicant Concentration (MATC) of Chemical A Technical was estimated to be < 0.062 mg AI/L, the lowest concentration tested.

b. Justification of deviation from acceptance criteria: although neither a NOEL nor a defined MATC was determined in this study, when these results are included with those of our previously submitted Fish Early Life Stage study on Chemical A, the Guideline requirement has been satisfied.

Table 1. Summary of statistical analysis of embryo viability, survival of embryos at hatch and survival, total length, and wet weight of rainbow trout (Salmo gairdneri) exposed to Chemical A for 88 days (60 days post-hatch).

Mean Measured Conc. (mg/L)	Embryo Viability (%)	Survival of Organisms at Hatch (%)	Larvae (60 days post-hatch)		
			Larvae Survival (%)	Mean Total Length (mm)	Mean Wet Weight (g)
.840 Mean					
.410 Mean					
.200 Mean					
.097 Mean					
.062 Mean					
Solvent Control Mean					
Control Mean					
Pooled Controls					

(In this sample, values have been omitted)

SAMPLE SUMMARY FOR TOXICOLOGY STUDIES

Phase 3 Summary of MRID 22222 and Related MRID 232323; Chronic Feeding of "HERBICIDE" in the Rodent: Project 23456

Guideline Reference:

83-1 Chronic Feeding in the Rodent and Nonrodent

Summary Prepared By:

J. Morrison, PhD.
March 15, 1980

Original Study Prepared By:

Unicorp Group Laboratories, Inc.
Providence, RI

Statement of No Data Confidentiality Claims

No claim of confidentiality is made for any information contained in this study on the basis of its falling within the scope of FIFRA section 10(d)(1)(A), (B), or (C).

Company:________________________________ (Typed Name)

Company Agent:________________________________ (Typed Name)

Title:________________________________

Signature:________________________________ Date:______________

Good Laboratory Practice Statement

This study meets the requirement for 40 CFR Part 160

Submitter of study:________________________________ (Signature)

Sponsor:________________________________ (Signature)

Study Director:________________________________ (Signature)

SAMPLE SUMMARY FOR TOXICOLOGY STUDIES

Certification of Availability of Raw Data

I hereby certify that the submitter possesses or has access to the raw data used in or generated by the study summarized in this document.

Submitter's Representative:

Signature/Date:______________________________

Typed Name:______________________________

Title:____________________

Certification of Accuracy of Summary and Adequacy of the Study

I certify, in compliance with FIFRA section 4(e)(1)(A), that this summary accurately represents the data presented in the report(s) of this study cited by MRID, and that this study fully satisfies all pertinent requirements of the OPP Guideline it addresses.

Submitter's Representative:

Signature/Date:______________________________

Typed Name:______________________________

Title:____________________

83-1 Chronic Feeding in the Rodent and Nonrodent

ACCEPTANCE CRITERIA

Does your study meet the following acceptance criteria?

1. Y Technical form of the active ingredient tested.
2. Y At least 20 rodents or 4 nonrodents/sex/group (3 test groups and control group).
3. Y Dosing duration in rodents minimum 12 month nonfood use, 24 months food use; in nonrodents minimum 12 months[1].
4. Y Doses tested include signs of toxicity at high dose but no lethality in nonrodents or a limit dose if nontoxic (1,000 mg/kg).
5.• Y Doses tested include a NOEL.
6.• Y Analysis for test material stability, homogeneity and concentration in dosing medium
7. Y Individual daily observations.
8. Y Individual body weights.
9. Y Individual or cage food consumption.
10.• Y Opthalmoscopic examination (at least pertest and at term) control and high dose.
11. Y Clinical pathology data for all nonrodents and at least 10 rodents/group consisting of 12, 13 & 14.
12. Y Hematology at 6 month intervals consisting of at least;
    Y Erythrocyte count
    Y Hemoglobin
    Y Hematocrit
    Y Leucocyte count
    • Y Differential count
    Y Platelet count (or clotting measure)
13. Y Clinical chemistry at 6 month intervals consisting of at least;
    • Y Alkaline phosphatase
    ____ Aspartate aminotransferase
    Y Alanine aminotransferase
    • Y Creatinine kinase
    • Y Lactic dehydrogenase
    Y Glucose
    Y Bilirubin
    • Y Cholesterol
    • Y Creatinine
    ____ Total Protein
    Y Albumin
    Y Urea nitrogen
    Y Inorganic phosphate
    ____ Calcium
    • Y Potassium
    Y Sodium
    • Y Chloride
14. Y Urinalysis at 6 month intervals consisting of at least;
    Y Blood
    Y Protein
    Y Ketone bodies
    Y Appearance
    Y Glucose
    Y Total bilirubin
    • Y Urobilirubin
    ____ Sediment
    Y Specific gravity (osmolality)
    • Y Volume
15. Y Individual necropsy of all animals.

Criteria marked with a • are supplemental and may not be required for every study.

16. ✓ Histopathology of the following tissues performed on all nonrodents and rodents, all control and high dose animals, all animals that died or were killed on study, all gross lesions on all animals, target organs on all animals and lungs, liver and kidneys on all other animals.

- ____ aorta
- ✓ eyes
- ✓ caecum
- ✓ colon
- ✓ duodenum
- ✓ brain†
- ____ skin
- ✓ heart
- ✓ testes†
- ✓ pituitary
- ✓ ileum
- ✓ trachea
- ____ gall bladder
- ✓ jejunum
- ✓ bone marrow
- ✓ liver†
- ✓ lung
- ✓ lymph nodes
- ✓ stomach
- ✓ mammary gland
- ✓ spleen
- ✓ musculature
- ✓ epididymis
- ✓ adrenals
- ✓ urinary bladder
- ✓ peripheral nerve
- ✓ kidneys†
- ✓ esophagus
- ✓ ovaries
- ✓ oviduct
- ✓ pancreas
- ____ rectum
- ✓ spinal cord (3x)
- ✓ thyroid / parathyroids
- ✓ salivary glands
- ✓ thymus
- ✓ accessory sex organs; uterus

† organs to be weighed

[1] In some cases, a six month study may be acceptable. Contact EPA to discuss the criteria for determining if such a study can be used to support reregistration.

Criteria marked with a * are supplemental and may not be required for every study.

SAMPLE SUMMARY FOR TOXICOLOGY STUDIES

83-1 Chronic Feeding Study in the Rodent and Nonrodent

1. Technical PESTICIDE (96.2%) was used.
2. Weaning SPF Sprague-Dawley rats (75/sex/dose) were fed diets containing 0, 100, 300 or 1,000 ppm technical pesticide.
3. Duration was 24 months.
4. At 1,000 ppm, the following effects were seen: increased mortality in females, (months 18.24); decreased weight gain in males (-15%) and females (-22%); ataxia, tremors, urogenital staining and lacramation in males and females; other effects in clinical chemistry and histopathy and will be discussed in those sections.
5. The 100 ppm dose levels was a NOEL for all parameters measured.
6. Test diet, prepared biweekly, was stable for 3 weeks with concentrations of 98.5±2, 101.3±3 and 96.2±2% for the test doses of 100, 300 and 1,000 ppm.
7. Increased mortality was observed in the high dose females in months 18-24. Signs of toxicity, including ataxia, tremors, urogenital staining and excessive lacrimation were seen in the 1,000 ppm males and the 300 and 1,000 ppm females. NOELs for all observations were 300 ppm for males and 100 ppm for females.
8. A dose-related decrease in weight gain was seen in the 300 and 1,000 ppm females and the 1,000 ppm males.
9.

Dose (ppm)	Food Consumption (g/Kg)		PESTICIDE dose (mg/Kg/day)	
	M	F	M	F
0	53.0	68.9	0.00	0.00
100	52.1	68.1	5.00	7.00
300	52.2	65.8	15.75	19.80
1000	54.8	77.2	54.69	77.19

10. Opthalmoscopic exams were not carried out, however since no adverse pathological lesions were noted in this study and the long-term rat and mouse study, it is doubtful that these opthalmoscopic exams would add much to the experiment.
11. Complete clinical pathology measurements were carried out on 10 rats/sex/dose at 6, 12, 18 and 24 months.
12. There were no dose-related effects on any hematogical measurements.
13. Clinical chemistry, as noted in the check list, showed increased alkaline phosphatase and lactic dehydrogenase in the females at 18 and 24 months at 1,000 ppm. No other effects were noted. Total protein, aspartate aminotransferase and

calcium were not determined.

14. No dose-related effects were noted on any urinalysis measurements. Although "sediment," per se, was not noted.
15. Gross necropsy of all rats showed stained/mottled liver in females at 300 and 1,000 ppm and in males at 1,000 ppm.
16. Increased absolute organ weights of brain, liver and kidneys were observed in females at 1,000 ppm whereas relative organ/body weight ratios were increased for liver and kidney. The only histopathological effect noted was necrosis in the livers of females at 300 and 1,000 ppm and males at 1,000 ppm. Histopathological exams of the aorta, skin and rectum were not carried out.
17. Deficiencies and their impact:

It is our opinion that the lack of measurements of the 3 parameters listed in criteria 13 have little affect on the final determination of the study. Other serum enzymes showed no adverse effects and histopathological exams were adequate to detect any abnormalities that would be signaled by changes in these parameters

It is our opinion that, although no specific observation for "sediment" was reported, that the comments and observations under appearance would be sufficient to detect the appearance of sediment in any urine samples.

Although histopathology exams of the aorta, skin and rectum were not done, gross observations failed to detect any significant abnormalities.

Phase 3 Summary of MRID 789878 and Related MRIDs 123212 and 234567; Makebelonate - Hydrolysis Study: Project 890234

Guideline Reference:

161-1 Hydrolysis

Summary Prepared By:

Henly Hankboro
November 15, 1980

ORIGINAL STUDY PERFORMED BY

Curie Chemistry Associates
Shreveport, LA

Statement of No Data Confidentiality Claims

No claim of confidentiality is made for any information contained in this study on the basis of its falling within the scope of FIFRA section 10(d)(1)(A), (B), or (C).

Company:________________________________ (Typed Name)

Company Agent:________________________________ (Typed Name)

Title:________________________________

Signature:________________________________ Date:______________

Good Laboratory Practice Statement

This study meets the requirement for 40 CFR Part 160

Submitter of study:____________________________ (Signature)

Sponsor:____________________________ (Signature)

Study Director:____________________________ (Signature)

Certification of Availability of Raw Data

I hereby certify that the submitter possesses or has access to the raw data used in or generated by the study summarized in this document.

Submitter's Representative:

Signature/Date:____

Typed Name:____

Title:____________________________

Certification of Accuracy of Summary and Adequacy of the Study

I certify, in compliance with FIFRA section 4(e)(1)(A), that this summary accurately represents the data presented in the report(s) of this study cited by MRID, and that this study fully satisfies all pertinent requirements of the OPP Guideline it addresses.

Submitter's Representative:

Signature/Date:____

Typed Name:____

Title:____________________________

161-1 Hydrolysis

ACCEPTANCE CRITERIA

Does your study meet the following acceptance criteria?

1. Y Test substance was the Technical Grade (TGAI) or a Pure Active Ingredient Radiolabeled (PAIRA).
2. Y Radiopurity and specific activity of Active Ingredient (AI) (if radiolabeled).
3. Y The positions of the AI radiolabeling were appropriate (if radiolabeled).
4. Y Solubility of the AI at each pH tested.
5. Y Concentration of AI (in solution) within the known solubility range of the AI and below 250 ppm
6. Y Study was conducted in darkness.
7. Y Temperature held at 25±1°C.
8. Y Sterility of glassware, reagents, chemicals, etc. was assured.
9. Y Volatiles (if any) were trapped.
10. Y Solutions were buffered.
11. Y Cosolvent (if any) did not exceed 1%.
12. Y pH of each test solution was reported and was correct (nominally 5,7 and 9) and constant.
13. Y Sampling intervals were adequate.

14.* Y Study was conducted for one half-life or 30 days.

15. Y A reasonable attempt was made to identify all degradates/hydrolysates which exceeded 10% (yield) of the initial concentration of the AI.
16. Y Material balance was reasonable (>90% -<110%).
17. Y Appropriate analytical methods provided.

18.* Y Detection limits were reported.

Criteria marked with a * are supplemental and may not be required for every study.

19. Y Half-lives were calculated.

Criteria marked with a * are supplemental and may not be required for every study.

SAMPLE SUMMARY FOR AN ENVIRONMENTAL FATE STUDY

HYDROLYSIS SUMMARY SHEET FOR MAKABELONATE (STOMPOUT)
GUIDELINE REFERENCE NO: 161-1

SUMMARY OF CONCLUSIONS

	pH5	pH7	pH9
Makabelonate hydrolysis T1/2:	120 da	88 da	72 da

Conclusion: Stable

TEST MATERIAL

IUPAC designation: 1,1-tetracarbamo-3-trichloro-nucleoside
CAS Number: 99999-99-0
Source: Synthetic Chemical Company
Lot Number: 123456-DDT
Formulation and Purity: TGAI, 94% AI, no identifiable impurities
Chemical class: oligopolycarbamochloronucleoside
Solubility: 100 mg/mL
Radioactive labeling site: Uniform, furocpuro ring
Specific activity: 600 uCi/mmole

TEST METHODOLOGY

Lighting conditions: Complete darkness
Temperature range: 20 ±
Spiked samples: 10, 100, 1000 mg/L efficiency = 98%
Water and characteristics: deionized water, filtered through a 0.22 micron Millipore filter, characteristics: pH=7.8; hardness, 140 mg as $CaCO_3$; alkalinity, 14 mg as $CaCO_3$; and conductivity, 700 umho.

Buffers used: pH 5, 0.1 mM acetate buffer
pH 7, 0.1 nM phosphate buffer
pH 9, 0.1 mM borate buffer
Cosolvent: None
Sampling intervals: Time zero, 1, 3, 7, and 14 days. Thereafter, samples were taken every 2 weeks.
Volatiles trap: A trap consisting of hyaminehydroxide-saturated filter paper was used to trap radioactive volatiles.
Sample extraction: Parent and degradate were extracted using a guideline-approved acidification method and dried on filter paper.

Extraction efficiency: Parent, 97%; Degradate, 97.5%

SAMPLE SUMMARY FOR AN ENVIRONMENTAL FATE STUDY

Sample stability:	Samples on filter paper were stored at -20 °C for up to a week before counting. Stability studies have shown that the samples are stable in this condition for up to a month.
Counting method:	Filter paper was immersed in PPO-POPOP cocktail and counted in a Packard Tricarb scintillation counter.

RESULTS

Materials balance - experimental

Parent - 98.4% of the added material
Degradate - 98.4% of the added material

Materials balance - Spiked samples

Parent - 99.7% of the added material
Degradate - 99.7% of the added material

T1/2 Determination method: Linear Regression - SYSTAT model

REGISTRANT CAN

PUT

GRAPHS

OR

TABLES

HERE

AT THEIR OPTION

DISCUSSION

AREA FOR
OPTIONAL
EXPLANATION
OF
STUDY DEVIATIONS

End

SAMPLE SUMMARY FOR RESIDUE CHEMISTRY STUDIES

Phase 3 Summary of MRID 888888;
Metabolism of "HERBICIDE" in Soybeans: Project 23489

Guideline Reference:

171-4(a) Nature of the Residue: Plant Study

Summary Prepared By:

A. Chemist
November 16, 1980

Original Study Prepared By:

XYZ Laboratory
Chicago, IL

Statement of Data Confidentiality Claims

Information claimed confidential on the basis of its falling within the scope of FIFRA §10(d)(1)(A), (B), or (C) has been removed to a confidential appendix, and is cited by cross-reference number in the body of the study.

Company:________________________________ (Typed Name)

Company Agent:________________________________ (Typed Name)

Title:________________________________

Signature:________________________________ Date:______________

Good Laboratory Practice Statement

This study does not meet the requirements of 40 CFR Part 160, and differs in the following ways:

1. ______________________________
2. ______________________________
3. ______________________________

Submitter of study:______________________ (Signature)

Sponsor:______________________ (Signature)

Study Director:______________________ (Signature)

SAMPLE SUMMARY FOR RESIDUE CHEMISTRY STUDIES

Certification of Availability of Raw Data

I hereby certify that the submitter possesses or has access to the raw data used in or generated by the study summarized in this document.

Submitter's Representative:

Signature/Date:______________________________________

Typed Name:______________________________________

Title:___________________________

Certification of Accuracy of Summary and Adequacy of the Study

I certify, in compliance with FIFRA section 4(e)(1)(A), that this summary accurately represents the data presented in the report(s) of this study cited by MRID, and that this study fully satisfies all pertinent requirements of the OPP Guideline it addresses.

Submitter's Representative:

Signature/Date:______________________________________

Typed Name:______________________________________

Title:___________________________

SAMPLE SUMMARY FOR RESIDUE CHEMISTRY STUDIES

Subdivision O
Guideline Ref. No. 171-4(a)
December 24, 1989

171-4(a) Nature Of The Residue – Plants Study

ACCEPTANCE CRITERIA

Does your study meet the following acceptance criteria?

1. Y Pesticide radiolabeled in non-labile portion of molecule (tritium label strongly discouraged)
2. Y Specific activity sufficient to permit detection of low residue levels (0.01-0.1 ppm range)
3. Y Radiochemically pure grade of active ingredient
4. Y Pesticide applied to plant in manner simulating expected use
5. Y Total radioactivity measured in plant parts used for human food or animal feed
6. Y Extractability of residue into solvents determined
7. Y Most of radioactivity extracted or exhaustive attempts (acid, base, enzyme) made to do so
8. Y Major components or portion of the terminal residue identified (preferably by at least two techniques-e.g., TLC, HPLC, MS)

Criteria marked with a * are supplemental and may not be required for every study.

171-4(a) Nature of the Residue: Plants Study

SUMMARY OF STUDY

1. Chemical structure and name of test material with site of radiolabel indicated.
   N-methyl-3-bromoaniline; also known as "HERBICIDE"
   The 14-C radiolabel was uniformly distributed through the phenyl ring. (See cross-reference number 1 in Confidential Attachment).

2. Specific activity of test material and detection limit achieved for treated commodities.
   Specific activity = 19.1 mCi/mg. The detection limits for treated soybean crop parts were 0.01-0.03 ppm.

3. Radiochemical purity of test material.
   The radiochemical purity of ^{14}C-HERBICIDE was 98.5%.

4. Description of formulation and application of test material and comparison of application (rate, timing in terms of growth stage of crop) to expected use of pesticide.
   Radiolabeled HERBICIDE was formulated as an emulsifiable concentrate by addition of the emulsifier and organic solvent used in the commercial product. The formulation was diluted with water and applied to the soybean foliage at the fourth-trifoliate stage at a rate equivalent to 0.25 pounds active ingredient per acre, twice the rate permitted on HERBICIDE labels. Soybeans would typically be in third to fourth-trifoliate stages when HERBICIDE is applied.

5-7. Description of procedures used to quantitate and extract radioactivity.
Total radioactivities of all plant parts were determined by combustion of aliquots to $^{14}CO_2$. Samples were washed with hexane followed by blending and extraction with 20% methanol in acetone. In the case of dry crop parts, refluxing with 1N HCl was used to release additional residues. The total ppm found in plant parts and the distribution of the residues in the various solvents are summarized at the top of the next page.
Extraction of the radioactivity in soybean seeds was not attempted due to the very low level of residue (<0.01 ppm).

8. Description of procedures used to identify radiolabeled residues.
   Hexane washes and acetone extracts were analyzed directly by

Crop part	PHI	14-C total	% into hexane	% into acetone	% into 1N HCl	% not released
Green plant	2	27.5	75	20	--	5
Dry leaves	75	13.8	15	44	28	13
Dry stalks	75	2.9	10	50	23	17
Pods	75	0.7	3	35	40	22

PHI=preharvest interval in days; 14-C in ppm HERBICIDE equivalents

thin layer chromatography and autoradiography. R_f values were compared to authentic standards. The HCl solutions were extracted with ether and the latter examined by TLC also. The identities of spots were further confirmed by scraping the spots from the plates and examining them by mass spectrometry. The residues on each crop part are summarized in the following table in which "TRR" is total radioactive residue, "4-hydroxy" refers to N-methyl-3-bromo-4-hydroxyaniline and "desmethyl" refers to 3-bromoaniline.

		% of TRR			
Crop part	Total 14-C	Parent	4-hydroxy	Desmethyl	Unidentd
Green plant	27.5 ppm	72%	12%	9%	7%
Dry leaves	13.8 ppm	24%	39%	11%	26%
Dry stalks	2.9 ppm	18%	42%	8%	32%
Pods	0.7 ppm	15%	27%	15%	43%

In all cases about half the unidentified residue was activity that could not be extracted by solvents or HCl. The remainder consisted of very polar materials based on their TLC behavior.

SAMPLE SUMMARY FOR RESIDUE CHEMISTRY STUDIES

CONFIDENTIAL ATTACHMENT

Phase 3 Summary of MRID 888888; Metabolism of "HERBICIDE" in Soybeans: Project 23489

Guideline Reference:

171-4(a) Nature of the Residue: Plant Study

Summary Prepared By:

A. Chemist
November 16, 1980

Original Study Prepared By:

XYZ Laboratory
Chicago, IL

SAMPLE SUMMARY FOR RESIDUE CHEMISTRY STUDIES

Cross Reference Number 1

This cross reference number is used in the study in place of the following words at the indicated page and line references.

DELETED WORDS: [identitiy of inert ingredients]

PAGE	LINE	REASON FOR THE DELETION	FIFRA REFERENCE
6	4	Identity of inert ingredient	10(d)(1)(C)

SUPPLEMENTAL STATEMENT OF DATA CONFIDENTIALITY CLAIMS

[AREA FOR SPECIFIC INFORMATION
SUPPORTING A CLAIM
OF CONFIDENTIALITY NOT
BASED ON
FIFRA 10(d)(1)(A), (B), OR (C)]

Signature/Date: ____________________

Typed Name: ____________________

Title: ________________

APPENDIX B: PR NOTICE 89-3

PR NOTICE 89-3

NOTICE TO REGISTRANTS SUBJECT TO REREGISTRATION PHASE 3

Attention:	Persons responsible for preparing Reregistration Phase 3 responses.
Subject:	Format standards for Reregistration Phase 3 summaries and reformatted versions of studies previously submitted under the Federal Insecticide, Fungicide and Rodenticide Act (FIFRA) and certain provisions of the Federal Food, Drug, and Cosmetic Act (FFDCA).

I. Purpose

To define standard formats for summaries and reformatted versions of previously submitted studies, as required to be submitted in Phase 3 of reregistration by section 4(e)(1) of FIFRA, as amended.

II. Applicability

This notice applies to all summaries of previously submitted data provided to the Agency under section 4(e)(1)(A) or (B) of FIFRA, and to all reformatted versions of previously submitted data provided under section 4(e)(1)(C) or (D) of FIFRA.

III. Effective Date

This notice is effective upon issuance.

IV. Background

The amendments to FIFRA of October, 1988 define a new five-phase program of reregistration. In the third of these five phases registrants of pesticides first registered before 1984 must submit structured summaries of all previously submitted studies on which they wish to rely to support reregistration, and must submit

Preceding page blank

complete reformatted versions of selected toxicology and residue studies as well.

The schedule for reregistration laid out in the amended Act requires that many thousands of these documents will arrive at the Agency over a very short time, and requires further that the Agency review them very soon after they arrive.

Thus it is critical to the success of the overall reregistration program that these summaries and reformatted studies be added to the Agency's master document management systems as rapidly and economically as possible. Toward that end these standards have been defined.

V. Relationship of this Notice to Other Policy and Guidance

This notice complements PR Notice 86-5, but does not supersede it. PR Notice 86-5 remains controlling with respect to all data submissions to OPP except those associated with Reregistration Phase 3.

This notice also complements the guidance called for in section 4(e)(4)(A) of amended FIFRA, which specifies content-related requirements for reregistration Phase 3 responses.

VI. Scope and Organization of the Phase 3 Submittal Package

The scope of a single Phase 3 submittal must be limited to a single registrant's submission for a single chemical within a single reregistration case. A Phase 3 submittal package consists of the following four elements, physically arranged in the order listed:

A. One signed and dated copy of the "Reregistration Phase 3 Chemical Response Worksheet", which serves as a transmittal document for all other components of the response (be sure not to include any information you claim as confidential in this document),

B. One copy of each summary of a previously submitted study shown to be 'provided' on the Worksheet/Transmittal, formatted as described in section VIII below,

C. One copy of each reformatted version of a previously submitted study shown to be 'provided' on the Worksheet/Transmittal, formatted as described in section IX below, and

D. One copy of any other correspondence or material submitted with the above elements in the package. (See the Phase 3 Guidance for more information about specific documents which would fall into this "other material" category, such as waiver requests and supporting rationales, discussions of applicability of individual data requirements, and the like.) Generally these documents should not need to contain any confidential business information. If you wish to make a claim of confidentiality for any information in any of these documents, the specific information covered by the claim and the basis for the claim must both be clearly identified.

In other words, a Phase 3 submittal consists of the worksheet/ transmittal, followed by all the summaries, followed by all the reformatted studies, followed by any other materials. This arrangement is illustrated in Attachment 3.

VII. Scope of a Study

The scope of one Phase 3 summary, or of one reformatted report, is a single study. As defined in PR Notice 86-5, a "study" is the report of a single scientific investigation, including all supporting analyses required for logical completeness. In determining the scope of a study for Phase 3 responses, take particular care to include all significant related documents, including supplements, addenda, supporting analyses and the like, even if they were previously submitted at a different time from the primary report of the study. One of the objectives of the requirement to summarize and reformat studies is to bring together all such partial or fragmentary reports of studies into well defined, logically complete new documents. Take care as well to summarize and reformat separately logically distinct studies which may have originally been submitted bound together in a single volume.

In most cases a study will correspond in scope to a single Guideline requirement. The following special considerations, however, deserve mention; note that these points reflect the same principles of study identification originally laid out in section C(1) of PR Notice 86-5.

When a single study (i.e., the report of a single investigation) addresses more than one Guideline topic, a separate summary should be prepared for each Guideline topic addressed. Each such summary derived from a single original study would, of course, cite the same original MRID.

In the case of product chemistry data, the scope of a single 'study' may be broadened when appropriate to include all guideline requirements within a single guideline series (such as series 61, 62, or 63.)

In the case of residue data, the scope of a single 'study' should be limited to a single analytical method, an investigation of the nature of the residue in a single plant or animal species, or to an investigation of the magnitude of residues resulting from treatment of a single crop or from processing a single crop. This is true for residue data originally submitted in broad, multiple topic volumes as well as for residue data originally submitted in more narrowly defined studies.

When multiple field trials are associated with a single investigation, the reports of all such trials should be treated as a single study.

VIII. Required Elements for Phase 3 Summaries

Most of the elements required for Phase 3 summaries are defined and discussed in PR Notice 86-5. The specific requirements for summaries and the order in which they must appear are as follows. These elements and their order are illustrated in Attachment 4.

A. Title Page. The first page of each summary must be a title page. The title page must not include any information claimed as confidential, and must include the following elements:

1. Title. The title of each Phase 3 summary must be in standard form, to make these summaries easy to recognize from citations. The required elements in the title are:

- the introductory words "Phase 3 Summary of MRID",
- the MRID assigned to the previously submitted primary report,
- if more than one previously submitted document is included in the scope of the summary, the MRIDs assigned to all other included reports,
- the descriptive title of the original study, and
- the performing laboratory's or submitter's study identification number or code, if any.

Represented schematically, with mandatory text in bold face, unconditionally required elements in square brackets, and conditional elements in curved brackets, the title of a Phase 3 summary would be:

> **Phase 3 Summary of MRID** [primary MRID] {and related MRIDs a, b, and c}: [Descriptive Title]: {Project Nr 123}.

Here is an example of a title conforming to these requirements:

> Phase 3 Summary of MRID 123456 and related MRIDs 141865 and 141866: Teratology of Technical Buggywhip to New Zealand Rabbits: Project Number 82-104.

2. **Guideline Reference Number** and **Name of Requirement.** Enter these elements on the title page exactly as they appear on the Phase 3 Worksheet.

3. **Author.** Identify the author of the summary, not the author of the original study being summarized.

4. **Date.** Include the date of the summary, not the date of the original study being summarized.

5. **Performing Laboratory.** Enter the name(s) and address(es) of all laboratories who performed or contributed to the original study. If more laboratories were involved than can be listed on the title page, include on the title page a reference to an internal page on which they all appear.

6. **Pagination.** Enter the phrase "Page 1 of x", where "x" is the total number of pages in the body of the summary, exclusive of the confidential attachment or supplemental statement of confidentiality claims, if any.

B. **Statement of Data Confidentiality Claims.** Page 2 of each Phase 3 summary must include one of the two standard statements of data confidentiality claims defined in section D(2) of PR Notice 86-5, either asserting that no claims of confidentiality under FIFRA section 10(d)(1)(A), (B), or (C) are made for the summary, or that information claimed confidential under that authority has all been removed from the body of the summary to a confidential attachment. Note that these statements apply only to confidentiality claims under FIFRA section 10(d)(1)(A), (B), or (C): that you will have no further opportunity to register claims of confidentiality not made at this time, and that the wording of the two forms of the statement is mandatory. You may add to either statement as appropriate, but the language specified must all be included and must not be altered or contradicted. This statement must be signed and dated by an authorized representative of the submitter.

C. **Statement of Good Laboratory Practice Compliance.** Page 3 of each Phase 3 summary must bear an appropriate statement concerning the compliance or non-compliance of the original study with EPA's Good Laboratory Practices regulations (40 CFR 160).

Note that while a statement of GLP compliance is always required, its wording is not prescribed. Since many of the studies summarized in Phase 3 will have been performed before these regulations were in place, a statement to that effect will often be all that is necessary or appropriate. See 40 CFR 160.12 for more information about this requirement.

Under the regulations the GLP compliance statement must be signed by the study director, the study sponsor, and the study submitter. Clear, legible photocopies of statements from the original study report are acceptable. If the study director or study sponsor is unavailable to sign a new statement, this should be explained in the statement, and it must be signed by the submitter.

D. Certification of Access to Raw Data. Two mandatory statements are required on page 4 of each Phase 3 summary. The first of them is a certification of access to raw data. (The second is discussed in paragraph E below.) The wording of the certification of access to raw data is mandatory, and it must be signed and dated by an authorized representative of the submitter:

Certification of Access to Raw Data

> I hereby certify that the submitter possesses or has access to the raw data used in or generated by the study summarized in this document.
>
> Submitter's Representative: [Signature/Date]
> [Typed Name]
> [Title]

E. Certification of Accuracy of Summary and Adequacy of the Study. The second certification required on page 4 of each Phase 3 summary is the appropriate one of the two following statements with respect to the accuracy of the summary and adequacy of the underlying study to satisfy Guideline requirements. Note that only one of these two statements is appropriate, that the wording of the certification is mandatory, and that either version must be signed and dated by an authorized representative of the submitter.

1. For use when the study fully satisfies the requirement:

> I certify, in compliance with FIFRA section 4(e)(1)(A), that this summary accurately represents the data presented in the report(s) of this study cited by MRID, and that this study fully satisfies all pertinent requirements of the OPP Guideline it addresses.
>
> Submitter's Representative: [Signature/Date]
> [Typed Name]
> [Title]

2. **For use when the study does not satisfy the requirement:**

I certify, in compliance with FIFRA section 4(e)(1)(B), that this summary accurately represents the data presented in the report(s) of this study cited by MRID. Although this study does not fully satisfy the requirements of the OPP Guideline it addresses, it should nonetheless be accepted in satisfaction of this Guideline requirement. The specific deficiencies of the study and the rationale for its acceptance in spite of those deficiencies are individually identified and discussed within this summary.

Submitter's Representative: [Signature/Date]
[Typed Name]
[Title]

F. Body of the Summary. This should be prepared as specified in the Phase 3 Guidance material appropriate to the Guideline topic addressed.

G. Confidential Attachment. The confidential attachment, if any, and its cover sheet, as defined in section D(3) of PR Notice 86-5, follow the body of the summary, within the same binding.

H. Supplemental Statement of Data Confidentiality Claims. A supplemental statement of data confidentiality claims based on authority other than FIFRA section 10(d)(1)(A), (B), or (C), if any, as defined in section D(4) of PR Notice 86-5, follows the confidential attachment to the summary, if any, or the body of the summary if there is no confidential attachment.

IX. Required Elements for Studies Reformatted in Phase 3

The elements required for studies reformatted in Phase 3 are very similar to those required for Phase 3 summaries. The specific requirements and the order in which they must appear in each reformatted study are as follows. These elements and their order are illustrated in Attachment 4.

A. Title Page. The first page of each study must be a title page. Do not include any information claimed as confidential on the title page. Do include the following elements:

1. **Title.** The title of each study reformatted in Phase 3 must be in standard form, to make these studies easy to recognize from citations. The required elements in the title are:

- the introductory words "Phase 3 Reformat of MRID",
- the MRID assigned to the previously submitted primary report,

- if more than one previously submitted document is included in the scope of the study, the MRIDs assigned to all other included reports,
- the descriptive title of the study, and
- the performing laboratory's or submitter's study identification number or code, if any.

Represented schematically, with mandatory text in bold face, unconditionally required elements in square brackets, and conditional elements in curved brackets, the title of a study reformatted in Phase 3 would be:

> **Phase 3 Reformat of MRID** [primary MRID] (and related MRIDs a, b, and c): [Descriptive Title]: (Project Nr 123).

Here is an example of a title conforming to these requirements:

> Phase 3 Reformat of MRID 123456 and related MRIDs 141865 and 141866: Teratology of Technical Buggywhip to New Zealand Rabbits: Project Number 82-104.

2. **Guideline Reference Number** and **Name of Requirement.** Enter these elements on the title page exactly as they appear on the Phase 3 Worksheet.

3. **Author.** Identify the author(s) of the original study.

4. **Date.** Report the date of the original study.

5. **Information about Reformatting.** Report the date of the reformat, and by whom it was done.

6. **Performing Laboratory.** Enter the name(s) and address(es) of all laboratories who performed or contributed to the original study. If more laboratories were involved than can be listed on the title page, include on the title page a reference to an internal page number on which they all appear.

7. **Pagination.** Enter the phrase "Page 1 of x", where "x" is the total number of pages in the body of the study, exclusive of the confidential attachment or supplemental statement of confidentiality claims, if any.

B. **Statement of Data Confidentiality Claims.** Page 2 of each Phase 3 study must include one of the two standardized statements of data confidentiality claims defined in section D(2) of PR Notice 86-5, either asserting that no claims of confidentiality under

FIFRA section 10(d)(1)(A), (B), or (C) are made for the study, or that information claimed confidential under that authority has all been removed from the body of the study to a confidential attachment. Note that these statements apply only to confidentiality claims under FIFRA section 10(d)(1)(A), (B), or (C); that you will have no further opportunity to register claims of confidentiality not made at this time; and that the wording of the two forms of the statement is mandatory. You may add to either statement as appropriate, but the language specified must all be included and must not be altered or contradicted. This statement must be signed and dated by an authorized representative of the submitter.

C. **Statement of Good Laboratory Practice Compliance.** Page 3 of each Phase 3 study must bear an appropriate statement concerning the compliance or non-compliance of the original study with EPA's Good Laboratory Practices regulations (40 CFR 160).

Note that while a statement of GLP compliance is always required, its wording is not prescribed. Since many of the studies reformatted in Phase 3 will have been performed before these regulations were in place, a statement to that effect will often be all that is necessary or appropriate. See 40 CFR 160.12 for more information about this requirement.

Under the regulations the GLP compliance statement must be signed by the study director, the study sponsor, and the study submitter. Clear, legible photocopies of appropriate statements from the original study report are acceptable. If the study director or study sponsor is unavailable to sign a new statement, this should be explained in the statement, and it must be signed by the submitter.

D. **Body of the Study.** This should be prepared as specified in the Phase 3 Guidance material appropriate to the Guideline topic addressed.

E. **Confidential Attachment.** The confidential attachment, if any, and its cover sheet, as defined in section D(3) of PR Notice 86-5, follow the body of the study within the same binding.

F. **Supplemental Statement of Data Confidentiality Claims.** A supplemental statement of data confidentiality claims based on authority other than FIFRA section 10(d)(1)(A), (B), or (C), if present, as defined in section D(4) of PR Notice 86-5, follows the confidential attachment to the study, if any, or the body of the study if there is no confidential attachment.

X. **Physical Format Requirements for Phase 3 Submissions**. With the exception of a reduction in the number of copies required (see paragraph D below), physical requirements for Phase 3 submissions correspond to those established in PR Notice 86-5.

A. **Size and Media.** Each document submitted in Phase 3 must be on uniform 8 1/2 by 11 inch white paper, printed on one side only in black ink, with high contrast and good resolution. Be especially careful to ensure legibility of photocopied materials and signatures. Do not submit Phase 3 materials in any media other than paper without specific instructions from EPA.

B. **Binding.** Each Phase 3 summary, or each reformatted Phase 3 study, must be separately bound. Confidential attachments and supplemental statements of data confidentiality must be included within the binding of the body of the summary or report. All bindings must be secure, but easily removable to permit microfilming.

C. **Pagination.** All pages of each summary or study must be continuously paginated, beginning with the required title page as page 1. The total number of pages in the body of the document must appear on the title page and all other pages. If a confidential attachment is present, the pagination should start over at page 1 on the cover page of the confidential attachment, and the total number of pages in the confidential attachment must appear on each of its pages. If a supplemental statement of data confidentiality claims is present, it, too, must be separately paginated.

D. **Number of Copies.** Only one copy is required of any Phase 3 response materials. Please do not submit extra copies for any reason.

XI. **Submission of Phase 3 Materials.** All Phase 3 submissions must be addressed to:

Reregistration Phase 3 Response
US EPA: Office of Pesticide Programs
P.O. Box 14890
Silver Spring MD 20910-4890

Note that this is a USPS postal box, which cannot accept deliveries by private courier. Please submit all Phase 3 responses via USPS; if you need a receipt, you may send responses by certified mail, return receipt requested. Please do not attempt to deliver Phase 3 responses to any other address. It is critical to efficient processing that these submissions all arrive at the same place, already separated from all the other materials directed to OPP.

XII. For Further Information contact by mail:

John M. Carley
US EPA: Office of Pesticide Programs (H7504C)
401 M Street SW
Washington DC 20460

or by courier:

Document Processing Desk
Attn: John M. Carley
Crystal Mall #2, Room 266
1921 Jefferson Davis Highway South
Arlington VA 22202

or by phone:

(703) 557-2315.

Allan S. Abramson

Allan S. Abramson, Director
Program Management and
Support Division

Attachment 1	Example Title Page for Phase 3 Summary
Attachment 2	Example Title Page for Reformatted Study
Attachment 3	Organization of Overall Phase 3 Submission Package
Attachment 4	Organization of Individual Summary or Reformat

Attachment 1

Example Title Page for Phase 3 Summary

Phase 3 Summary of MRID 123456 and Related MRIDs 234567, 245678, and 245679: Teratology of Buggywhip to Albino Rabbits: Project 98765.

Guideline Reference:

83-3(b): Teratogenicity/Rabbit

Summary Prepared by

Able B. Charles, PhD.
April 1, 1990

Original Study Prepared by:

Extraordinary Laboratories, Inc.
Kennebunkport, Maine

In Cooperation with:

Arcane Consulting Specialists, Inc.
Port Townsend, Washington

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Example Title Page for Reformatted Study

Phase 3 Reformat of MRID 123456 and Related MRIDs 234567, 245678, and 245679: Teratology of Buggywhip to Albino Rabbits: Project 98765.

Guideline Reference:

83-3(b): Teratogenicity/Rabbit

Study Authors:

David E. Farmer
Georgeanne H. Incaviglia
James K. Lamb

Original Study Date:

March 15, 1979

Prepared by:

Extraordinary Laboratories, Inc.
Kennebunkport, Maine

In Cooperation with:

Arcane Consulting Specialists, Inc.
Port Townsend, Washington

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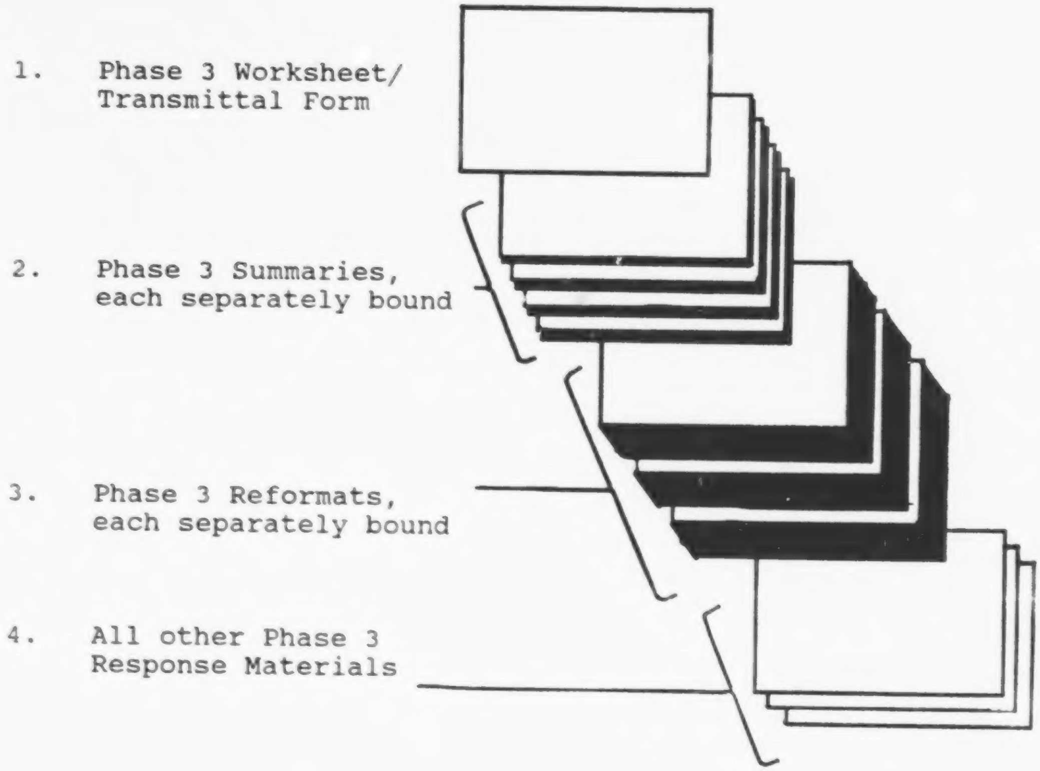
Attachment 3

Organization of Overall Phase 3 Submission Package:


1. Phase 3 Worksheet/ Transmittal Form
2. Phase 3 Summaries, each separately bound
3. Phase 3 Reformats, each separately bound
4. All other Phase 3 Response Materials

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Attachment 4

Organization of Individual Summary or Reformat
(All within same binding)

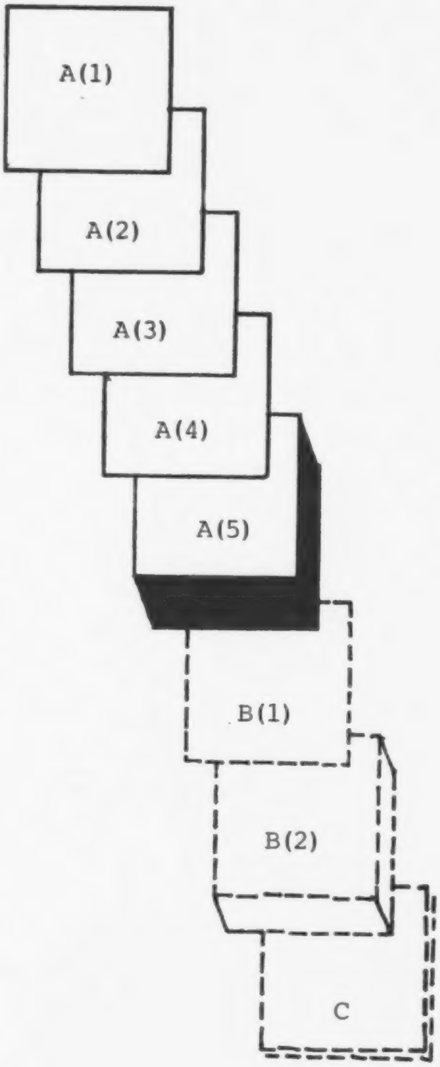
A. Mandatory Elements:

1. Title Page (page 1 of x)
2. Statement of Data Confidentiality Claims (page 2 of x)
3. GLP Compliance Statement (page 3 of x)
4. Certifications of Access to Raw Data and of Accuracy/Adequacy (page 4 of x)
5. Body of Summary or Study (pages 5 of x thru x of x)

B. Optional Elements--present only when Section 10(d)(1) Confidentiality Claims made:

1. Cover Sheet for Confidential Attachment (page 1 of y)
2. Body of Confidential Attachment (pages 2 of y thru y of y)

C. Optional Supplemental Claims of Data Confidentiality (pages 1 of z thru z of z)



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APPENDIX C: SPECIFIC GUIDANCE BY GUIDELINE REFERENCE NUMBER

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SUBDIVISION D

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Subdivision D
Guideline Ref. No. 61
December 24, 1989

61 Product Identity and Composition

ACCEPTANCE CRITERIA

Does your study meet the following acceptance criteria?

1. ___ Name of technical material tested (include product name and trade name, if appropriate)
2. ___ Name, nominal concentration, and certified limits (upper and lower) for each active ingredient and each intentionally-added inert ingredient
3. ___ Name and upper certified limit for each impurity or each group of impurities present at $\geq$ 0.1% by weight and for certain toxicologically significant impurities (e.g., dioxins, nitrosamines) present at $<0.1\%$
4. ___ Purpose of each active ingredient and each intentionally-added inert
5. ___ Chemical name from Chemical Abstracts Index of Nomenclature and Chemical Abstracts Service (CAS) Registry Number for each active ingredient and, if available, for each intentionally-added inert
6. ___ Molecular, structural, and empirical formulas, molecular weight or weight range, and any company assigned experimental or internal code numbers for each active ingredient
7. ___ Description of each beginning material in the manufacturing process
   ___ EPA Registration Number if registered; for other beginning materials, the following:
   ___ Name and address of manufacturer or supplier
   ___ Brand name, trade name or commercial designation
   ___ Technical specifications or data sheets by which manufacturer or supplier describes composition, properties or toxicity
8. ___ Description of manufacturing process
   ___ Statement of whether batch or continuous process
   ___ Relative amounts of beginning materials and order in which they are added
   ___ Description of equipment
   ___ Description of physical conditions (temperature, pressure, humidity) controlled in each step and the parameters that are maintained
   ___ Statement of whether process involves intended chemical reactions
   ___ Flow chart with chemical equations for each intended chemical reaction
   ___ Duration of each step of process
   ___ Description of purification procedures
   ___ Description of measures taken to assure quality of final product
9. ___ Discussion of formation of impurities based on established chemical theory addressing (1) each impurity which may be present at $\geq$ 0.1% or was found at $\geq$ 0.1% by product analyses and (2) certain toxicologically significant impurities (see #3)

Criteria marked with a * are supplemental and may not be required for every study.

61 Product Identity and Composition

GUIDANCE FOR SUMMARIZING STUDIES

The following criteria apply to the technical grade of the active ingredient being reregistered. Items 1, 2, 3, and 5 can be satisfied for most registered products by submission of the Certified Statement of Formula Ingredients Page (EPA Form 8570-4). Items 7 and 8 can be satisfied for most technical grade active ingredients (TGAIs) by submission of a flow chart with chemical equations for each intended chemical reaction. The flow chart should include complete chemical structures and names for each reactant and product of all the reactions.

Items in summary should include the items discussed in Chapter 2 of this package and the specific items listed below.

1. Name of technical material (include product name and trade name, if appropriate).
2. Description of each active and intentionally-added inert ingredient, including name, concentration, and certified limits.
3. Name and upper limit for all impurities present at $\geq 0.1\%$ and those toxicologically significant impurities present at $<0.1\%$.
4. The purpose of each active and intentionally-added inert ingredient.
5. Chemical name and Registry Number for each active and intentionally-added inert ingredient (if available).
6. Molecular, structural, and empirical formulas, molecular weight, and any experimental or internal code number for each active ingredient.
7. Description of each beginning material in the manufacturing process.
8. Description of manufacturing process.
9. Discussion of formation of impurities based on established chemical theory.

62 Analysis and Certification of Product Ingredients

ACCEPTANCE CRITERIA

The following criteria apply to the technical grade of the active ingredient being reregistered. Use a table to present the information in items 6, 7, and 8.

Does your study meet the following acceptance criteria?

1. ___ Five or more representative samples (batches in case of batch process) analyzed for each active ingredient and all impurities present at ≥ 0.1%
2. ___ Degree of accountability or closure ≥ ca 98%
3. ___ Analyses conducted for certain trace toxic impurities at lower than 0.1% (examples, nitrosamines in the case of products containing dinitroanilines or containing secondary or tertiary amines/alkanolamines plus nitrites; polyhalogenated dibenzodioxins and dibenzofurans) [Note that in the case of nitrosamines both fresh and stored samples must be analyzed.]
4. ___ Complete and detailed description of each step in analytical method used to analyze above samples
5. ___ Statement of precision and accuracy of analytical method used to analyze above samples
6. ___ Identities and quantities (including mean and standard deviation) provided for each analyzed ingredient
7. ___ Upper and lower certified limits proposed for each active ingredient and intentionally added inert along with explanation of how the limits were determined
8. ___ Upper certified limit proposed for each impurity present at ≥ 0.1% and for certain toxicologically significant impurities at <0.1% along with explanation of how limit determined
9. ___ Analytical methods to verify certified limits of each active ingredient and impurities (latter not required if exempt from requirement of tolerance or if generally recognized as safe by FDA) are fully described
10. ___ Analytical methods (as discussed in #9) to verify certified limits validated as to their precision and accuracy

Criteria marked with a * are supplemental and may not be required for every study.

62 Analysis and Certification of Product Ingredients

GUIDANCE FOR SUMMARIZING STUDIES

The following criteria apply to the technical grade of the active ingredient being reregistered.

Items in summary should include the items discussed in Chapter 2 of this package and the specific items listed below.

1. Number of representative samples analyzed for all active ingredients and all impurities present at ≥ 0.1%.
2. Degree of accountability or closure in analyses in item #1.
3. Chemical names of toxic impurities which were analyzed for levels <0.1%.
4. Brief description(s) of analytical method(s) used to measure active ingredients and impurities in items #1 and #3.
5. Statement of precision and accuracy of method(s) in item #4.
6. Chemical name and quantities observed (range, mean, standard deviation) for each ingredient (actives and impurities) analyzed in item #1.
7. Proposed upper and lower certified limits for each active ingredient and intentionally added inert with brief explanation of how limits were determined.
8. Proposed upper certified limit for each impurity present at >=0.1% and certain toxicologically significant impurities at <0.1% with brief explanation of how limits were determined.
9. Brief description of analytical method(s) used to verify certified limits (if same methods as item #4, may reference latter).
10. Statement of precision and accuracy of method(s) in item #9 (may reference item #5 if applicable).

63 Physical and Chemical Characteristics

ACCEPTANCE CRITERIA

The following criteria apply to the technical grade of the active ingredient being reregistered.

Does your study meet the following acceptance criteria?

63-2 Color
    ___ Verbal description of coloration (or lack of it)
    ___ Any intentional coloration also reported in terms of Munsell color system

63-3 Physical State
    ___ Verbal description of physical state provided using terms such as "solid, granular, volatile liquid"
    ___ Based on visual inspection at about 20-25°C

63-4 Odor
    ___ Verbal description of odor (or lack of it) using terms such as "garlic-like, characteristic of aromatic compounds"
    ___ Observed at room temperature

63-5 Melting Point
    ___ Reported in °C
    ___ Any observed decomposition reported

63-6 Boiling Point
    ___ Reported in °C
    ___ Pressure under which B.P. measured reported
    ___ Any observed decomposition reported

63-7 Density, Bulk Density, Specific Gravity
    ___ Measured at about 20-25°C
    ___ Density of technical grade active ingredient reported in g/ml or the specific gravity of liquids reported with reference to water at 20°C. [Note: Bulk density of registered products may be reported in lbs/ft^3 or lbs/gallon.]

63-8 Solubility
    ___ Determined in distilled water and representative polar and non-polar solvents, including those used in formulations and analytical methods for the pesticide
    ___ Measured at about 20-25°C
    ___ Reported in g/100ml (other units like ppm acceptable if sparingly soluble)

Criteria marked with a * are supplemental and may not be required for every study.

63-9 Vapor Pressure

___ Measured at ≈25°C (or calculated by extrapolation from measurements made at higher temperature if pressure too low to measure at 25°C)
___ Experimental procedure described
___ Reported in mm Hg (torr) or other conventional units

63-10 Dissociation Constant

___ Experimental method described
___ Temperature of measurement specified (preferably about 20-25°C)

63-11 Octanol/water Partition Coefficient

___ Measured at about 20-25°C
___ Experimentally determined and description of procedure provided (preferred method-45 Fed. Register 77350)
___ Data supporting reported value provided

63-12 pH

___ Measured at about 20-25°C
___ Measured following dilution or dispersion in distilled water

63-13 Stability

___ Sensitivity to metal ions and metal determined
___ Stability at normal and elevated temperatures
___ Sensitivity to sunlight determined

Criteria marked with a * are supplemental and may not be required for every study.

63 Physical and Chemical Characteristics

GUIDANCE FOR SUMMARIZING STUDIES

The following criteria apply to the technical grade of the active ingredient being reregistered.

Items in summary should include the items discussed in Chapter 2 of this package and the specific items listed below.

1. Description of color.
2. Description of physical state.
3. Description of odor.
4. Indication of melting point (in °C).
5. Indication of boiling point (in °C).
6. Indication of density, bulk density, and specific gravity.
7. Indication of solubility.
8. Indication of vapor pressure.
9. Indication of dissociation constant.
10. Indication of octanol/water partition coefficient.
11. Indication of pH.
12. Description of stability.

SUBDIVISION E

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71-1 Acute LD50 Test for Waterfowl and Upland Game Birds

ACCEPTANCE CRITERIA

The Agency will accept in fulfillment of this requirement a citation by the registrant of an appropriate study cited in one of the publications listed below. To be considered appropriate, a study must be conducted on the species and age of animal stipulated in the acceptance criteria, and must employ the form of chemical designated by the acceptance criteria. If a study that appears in any of the documents listed below meets those criteria, a registrant may be exempted from summarizing the study if the registrant submits a photocopy of the title page from the publication and a photocopy of the summarized study report from the publication. The publications that list studies acceptable to EPA are:

U.S. Department of the Interior, Manual of Acute Toxicity: Interpretation and Data Base for 410 Chemicals and 66 Species of Freshwater Animals; Fish and Wildlife Service, Resource Publication 160

U.S. Department of the Interior, Handbook of Toxicity of Pesticides to Wildlife; Fish and Wildlife Service, Resource Publication 153

U.S. Department of the Interior, Lethal Dietary Toxicities of Environmental Pollutants to Birds; Fish and Wildlife Service, Resource Publication 191

U.S. EPA, Acute Toxicity Handbook of Chemicals to Estuarine Organisms; Office of Pesticides and Toxic Substances; EPA/600/X-86/231; September 1986.

Does your study meet the following acceptance criteria?

GENERAL INFORMATION

1. ___ Date of test initiation and termination reported

MATERIALS/METHODS

2. Test birds
    - ___ Mallard duck or bobwhite quail tested
    - ___ Rationale for selection of species if the species used is different than that preferred in Subdivision E
    - ___ Age at the beginning of the test is at least 16 weeks old
    - *___ Method of selection of the sex of the birds described and sex ratio given

3. Breeding history
    - *___ History of the colony, including observed diseases or other medical problems and treatment of diseases
    - *___ Indicates if all of the birds are from the same hatch, pen reared, previously mated or unmated, phenotypically similar to wild counterpart, in a reproductive state brought on artificially, and identifies the individuals

Criteria marked with a * are supplemental and may not be required for every study.

4. Pretest period described
*______Acclimation period (days)
*____ Pretest diet, including identification and composition plus any antibiotics, vitamins, or food additives added to the feed
*____ Housing conditions, including number of animals/cage, ambient temperature and humidity, photoperiod and lighting, and source of feed and water
*____ Health, including mortality, sickness, and weight loss
____ Fasting period (hours)

5. Dosage described
____ Amount of test material dosed/bird
____ Method of administration (vehicle control/treatment), including oral intubation and size and type of capsule, if used
*____ Rationale for selection of method, route, or frequency, if different from that recommended in Subdivision E

6. Methods described
____ Number of treatment levels with a minimum of 5
____ Number of birds/treatment level and control(s) (10)
____ Method of assigning birds to treatment levels and control groups
____ Method used to determine treatment levels
____ Size of cages, including height, width, and length in cm
____ Number of birds/cage
____ Number of controls
____ Type of controls, including solvent, carrier, and whether negative or positive

7. Pens described
____ Location, including whether indoors or outdoors
*____ For indoor pens, ambient temperature, humidity, photoperiod, and lighting recorded
____ Source and availability of feed and water identified

8. Additional factors and observations described
____ Diet and any antibiotics, vitamins, or food additives added to the feed described
____ Schedule and methods for gross necropsy examinations described, if performed
*____ Tissue necropsies listed, if performed
____ Length of total observation period (minimum of 14 days) identified
____ Frequency of each observation identified
____ Bird weights reported, including when and how determined
____ Food consumption data for treated and control birds reported
*____ Technical terminology used to describe signs of intoxication defined
*____ Criteria for determining effects described

Criteria marked with a * are supplemental and may not be required for every study.

DISCUSSION AND RESULTS

9. ___ Include LD50 value in mg/kg with 95% confidence limits; the slope of the dose response line, if the method provides the slope; and the no-observed-effect level if determined. Raw mortality data provided.

10. ___ Description of the nature, incidence, time of occurrence, severity, and duration of all observed toxic effects, including death and any other abnormal or unusual signs and symptoms. For example, report any specific signs of intoxication associated with death and the time of onset and remission of toxic signs. Also report marked observations of fecal material.

11. ___ Gross pathological changes as noted by gross necropsies examination described.

12.*___ Control bird parameters, behavior, and general health which appear atypical are described.

13. ___ Statistical method referenced.

14. The relationship between the results of the study and the test chemical described, including
    ___ Obvious problems that occurred during the study as well as the effect, if any, these problems had on the outcome of the study
    ___ Rationale for major deviations from the protocol

15.*___ Graphs, printouts, and other calculations attached to the report

Criteria marked with a * are supplemental and may not be required for every study.

71-1 Acute LD50 Test for Waterfowl and Upland Game Birds

GUIDANCE FOR SUMMARIZING STUDIES

Items in summary should include the items discussed in Chapter 2 of this package and the specific items listed below.

GENERAL INFORMATION

1. Conclusions summarized, including date of test initiation and termination.

MATERIALS/METHODS

2. Description of test birds, including
   - Species tested (scientific and common names)
   - Rationale for selection of species, if species used is different than that preferred on Subdivision E
   - Age at the beginning of test for each species
   - Sex ratio

3. Description of breeding history, including
   - Whether the birds were from the same hatch, pen reared, and previously mated
   - Identification of individuals

4. Description of the pretest period, including
   - Fasting period (hours)

5. Description of dosage, including
   - Method of administration (vehicle control/treatment)
   - Rationale for selection of method, route, or frequency, if different from that recommended in Subdivision E

6. Description of methods, including
   - Number of treatment levels
   - Number of birds/treatment level and control(s)
   - Number of birds/cage
   - Number of controls
   - Type of controls, including solvent, carrier, and whether negative or positive

7. Description of pens, including
   - Location, including whether indoors or outdoors

8. Description of additional factors and observations, including
   - Length of total observation period (number of days)

DISCUSSION AND RESULTS

9. **Results, including**
   - Statistical method referenced
   - **LD50 value (mg/kg) with 95% confidence limits**
   - **The no-observed-effect level, if determined**
   - Bird weights reported, including when determined
   - **Food consumption data for treated and control birds**

10. Discussion relating the results of the study to test chemical, including
    - An explanation of obvious problems that occurred during the study and what effect, if any, these problems had on the outcome of the study.
    - The rationale for any major deviations from recommended protocol.

71-2 Acute Dietary LC50 Test for Waterfowl and Upland Game Birds

ACCEPTANCE CRITERIA

The Agency will accept in fulfillment of this requirement a citation by the registrant of an appropriate study cited in one of the publications listed below. To be considered appropriate, a study must be conducted on the species and age of animal stipulated in the acceptance criteria, and must employ the form of chemical designated by the acceptance criteria. If a study that appears in any of the documents listed below meets those criteria, a registrant may be exempted from summarizing the study if the registrant submits a photocopy of the title page from the publication and a photocopy of the summarized study report from the publication. The publications that list studies acceptable to EPA are:

U.S. Department of the Interior, Manual of Acute Toxicity: Interpretation and Data Base for 410 Chemicals and 66 Species of Freshwater Animals; Fish and Wildlife Service, Resource Publication 160

U.S. Department of the Interior, Handbook of Toxicity of Pesticides to Wildlife; Fish and Wildlife Service, Resource Publication 153

U.S. Department of the Interior, Lethal Dietary Toxicities of Environmental Pollutants to Birds; Fish and Wildlife Service, Resource Publication 191

U.S. EPA, Acute Toxicity Handbook of Chemicals to Estuarine Organisms; Office of Pesticides and Toxic Substances; EPA/600/X-86/231; September 1986.

Does your study meet the following acceptance criteria?

GENERAL INFORMATION

1. ____ Date of test initiation and termination reported

MATERIALS/METHODS

2. Preparation of test diets (control/treatment) described
    ____ Any vehicle used to dissolve or dilute test substance with the feed
    ____ Amount of vehicle added to control diet
    *____ Description of test diet and any other ingredients such as antibiotics, vitamins, or food additives which may have been in the feed preceding or during testing
    *____ Type of mixer and method of mixing in the test material and vehicle
    *____ Report data if food was analyzed for the pesticide concentration
    ____ Method used to determine concentration levels

Criteria marked with a * are supplemental and may not be required for every study.

3. Test birds
    ____ Mallard duck and bobwhite quail tested
    ____ Rationale for selection of species if the species used is different than that preferred in Subdivision E
    ____ Age at the beginning of the test is 5 to 10 days old for mallard ducks and 10 to 14 days for bobwhite quail

4. Breeding history
    ____ Birds were phenotypically similar to wild counterpart, all from the same hatch, and pen reared.
    ____ Any observed diseases and treatments were reported

5. Description of any pretest conditioning
    •____ Health
    •____ Description of pretest diet, including any antibiotics, vitamins, or food additives
    •____ Housing conditions described, including number of animals/cage, ambient temperature and humidity, photoperiod and lighting, and source of feed and water

6. Pen facilities described
    ____ Dimensions of test pen(s) in cm
    ____ Temperature (C°) and relative humidity
    ____ Photoperiod and lighting
    ____ Pen locations (indoors and outdoors)
    •____ Pen construction materials
    ____ Availability of water throughout the test
    •____ Provisions for ventilation

7. Concentration and dosage mortality/effects data
    ____ Method of identifying treatment levels
    ____ Description of the steps taken to maintain the concentration(s), if the test substance is administered in the feed, and if over the length of the test concentrations may decrease by 30% or more
    ____ Number of concentrations (5 or 6)
    ____ Number of days on test material (5)
    ____ Number of days on food free of test material (3)
    ____ Number of birds/cage
    ____ Number of birds/concentration and control group(s) (10)
    ____ Method for assigning test organisms to test and control groups (random)

8.•____ Methods for determining bird body weights or other physiological measurements described

9.•____ Food consumption - collection methods

Criteria marked with a • are supplemental and may not be required for every study.

10. Observations
- ____ Frequency of observations
- ____ Signs of intoxication and abnormal behavior
- ____ Palatability or repellency
- *____ List tissue necropsied, if performed
- *____ Criteria for determining effects
- *____ Define technical terminology used to describe signs of intoxication

DISCUSSION AND RESULTS

11. ____ Include LC50 value in ppm with 95% confidence limits; the slope of the dose response line, if the method provides the slope; and the no-observed-effect level if determined. Raw mortality data provided.

12.*____ Gross pathological changes as noted by gross necropsies examination, including characterization of gross lesions.

13. ____ Description of the nature, incidence, time of occurrence, severity, and duration of all observed toxic effects, including death and any other abnormal or unusual signs and symptoms. For example, report any specific signs of intoxication associated with death and the time of onset and remission of toxic signs. Also report marked observations of fecal material.

14. ____ Statistical method referenced.

15. The relationship between the results of the study and the test chemical described, including
- ____ Obvious problems that occurred during the study as well as the effect, if any, these problems had on the outcome of the study
- ____ Rationale for major deviations from the protocol

16.*____ Graphs, printouts, and other calculations attached to the report.

Criteria marked with a * are supplemental and may not be required for every study.

71-2 Acute Dietary LC50 Test for Waterfowl and Upland Game Birds

GUIDANCE FOR SUMMARIZING STUDIES

Items in summary should include the items discussed in Chapter 2 of this package and the specific items listed below.

GENERAL INFORMATION

1. Conclusions summarized, including date of test initiation and termination.

MATERIALS/METHODS

2. Description of test diet (control/treatment) preparation, including
    - Any vehicle used to dissolve or dilute test substance with the feed
3. Description of test birds, including
    - Species tested (scientific and common names)
    - Rationale for selection of species, if species used is different than that preferred on Subdivision E
    - Age at the beginning of test for each species
4. Description of breeding history, including
    - Whether the birds are from the same hatch and pen reared
5. Description of any pretest conditioning
6. Description of pen facilities, including
    - Pen locations (indoors and outdoors)
7. Description of concentration and dosage mortality/effects data, including
    - Number of concentrations
    - Number of days on test material
    - Number of days on food free of test material
    - Number of birds/cage
    - Number of birds/concentration and control group(s)
8. Description of observations, including
    - Frequency of observations

DISCUSSION AND RESULTS

9. **Results, including**
   - **Statistical method referenced**
   - **LC50 value (ppm) with 95% confidence limits**
   - **The no-observed-effect level if determined**
   - **Signs of intoxication and abnormal behavior**
   - **Palatability or repellency**

10. **Discussion relating the results of the study to test chemical, including**
    - **An explanation of obvious problems that occurred during the study and what effect, if any, these problems had on the outcome of the study.**
    - **The rationale for any major deviations from recommended protocol.**

71-3 Wild Mammal Toxicity Test

ACCEPTANCE CRITERIA

Does your study meet the following acceptance criteria?

GENERAL INFORMATION

1. ____ Date of test initiation and termination reported

MATERIALS/METHODS

2. Preparation of test material (control/treatment) described
   - ____ The vehicle used to dissolve test material
   - ____ Amount of vehicle added to the control
   - ____ Method used to get test material into diet
   - ____ Total amount of test material used

3. Test mammal
   - ____ Rationale for selection of species if the species used is different than those exposed to test substance's use pattern
   - ____ Test species common and scientific name
   - *____ History of test organisms (strain, disease, and treatment)

4. Pretest conditioning described
   - ____ Health, including sickness, injuries, abnormalities, name of medication (if used), and pretest diet
   - ____ Quarantine, including number of days mammals held

5. Size/age/physical condition described
   - ____ Age of each animal and how determined
   - ____ Size of the animal, including the weight of any animal more than ± 20% of mean weight
   - ____ Physical condition of test animals

Criteria marked with a * are supplemental and may not be required for every study.

6. Acclimation
*____ Daily food consumption
*____ Daily behavior of test animal
____ Body weights, including at the beginning and end of acclimation
____ Diet used
____ Source of animal food and water
____ Dimensions of pen(s)
*____ Length of photoperiod

7. Physical characteristics of testing facility described
____ Identification of any special laboratory equipment unique to the study

8. Biological characteristics of testing facility described
____ Daily temperature measurements
*____ Daily relative humidity measurements
____ Daily photoperiod
*____ Daily laboratory air exchange rate

9. Range finding test as the test exposure parameter
____ Number of animals used
*____ Method used to determine dose levels
____ Raw data for determining the end point
____ Treatment and observation period
____ Any statistical analysis utilized

10. Definitive test
____ Number of animals used and a rationale for using less than 10 animals per treatment level, if appropriate
____ Number of treatment levels
____ Name of vehicle used
*____ References to toxicity of vehicle
____ Controls and vehicle controls used
____ Raw mortality or effects data for each group
____ Duration of treatment and observation periods
____ Statistical analysis of the data
____ Methodology for dosing
____ Methodology for treatment diet preparation
____ Toxicologically related behavioral change
____ Analysis of basal diet
____ Criteria for end point of study
____ Number of animals of each sex of animal tested

11. ____Gross necropsies conducted

Criteria marked with a * are supplemental and may not be required for every study.

DISCUSSION AND RESULTS

12. Body weight and food consumption
    *____ Daily body weight by animal and level
    *____ Total daily food consumption by animal and level
    ____ Mean body weight for each test and control group at initiation and termination of test

13. ____ LC50 value in ppm with 95% confidence limits; the slope of the dose response line, if the method provides the slope; and the no-observed-effect level, if determined. Raw mortality data provided.

14. ____ Description of the nature, incidence, time of occurrence, severity, and duration of all observed toxic effects, including death and any other abnormal or unusual signs and symptoms. For example, report any specific signs of intoxication associated with death and the time of onset and remission of toxic signs. Also report marked observations of fecal material and urine.

15. ____ Gross pathological changes as noted by gross necropsies examination described.

16. ____ Control mammal response, behavior, and general health.

17. ____ Statistical method referenced.

18. The relationship between the results of the study and the test chemical described, including
    ____ Obvious problems that occurred during the study as well as the effect, if any, these problems had on the outcome of the study.

19.*____ Graphs, printouts, and other calculations attached to the report

Criteria marked with a * are supplemental and may not be required for every study.

71-3 Wild Mammal Toxicity Test

GUIDANCE FOR SUMMARIZING STUDIES

Items in summary should include the items discussed in Chapter 2 of this package and the specific items listed below.

GENERAL INFORMATION

1. Conclusions summarized, including date of test initiation and termination.

MATERIALS/METHODS

2. Description of test material (control/treatment) preparation, including
   - The vehicle used to dissolve test material

3. Description of test mammal, including
   - Rationale for selection of species if the species used is different than those exposed to test substance's use pattern
   - Species tested (common and scientific names)
   - History of test organisms (strain, disease, and treatment)

4. Description of pretest conditioning, including
   - Health, including sickness, injuries, abnormalities, name of medication (if used), and pretest diet
   - Quarantine, including number of days mammals held

5. Description of size/age/physical condition, including
   - Age of each animal and how determined
   - Size of the animal, including the weight of any animal more than ± 20% of mean weight
   - Physical condition of test animals

6. Description of acclimation, including
   - Diet used

7. Description of physical characteristics of testing facility, including
   - Identification of any special laboratory equipment unique to the study

8. Description of definitive test, including
    - Number of animals used and a rationale for using less than 10 animals per treatment level, if appropriate
    - Number of treatment levels
    - Name of vehicle used
    - References to toxicity of vehicle
    - Controls and vehicle controls used
    - Statistical analysis of the data
    - Methodology for dosing
    - Toxicologically related behavioral change
    - Number of animals of each sex of animal tested

9. Description of gross necropsies conducted

DISCUSSION AND RESULTS

10. Results, including
    - Statistical method referenced
    - LC50 value (ppm) with 95% confidence limits
    - The no-observed-effect level, if determined
    - Gross pathological changes as noted by gross necropsies examination
    - Control mammal response, behavior, and general health.
    - Mean body weight and food consumption for each test and control group at initiation and termination of test

11. Discussion relating the results of the study to test chemical, including
    - An explanation of obvious problems that occurred during the study and what effect, if any, these problems had on the outcome of the study.

71-4 Avian Reproduction Test for Waterfowl and Upland Game Birds

ACCEPTANCE CRITERIA

Does your study meet the following acceptance criteria?

GENERAL INFORMATION

1. ____ Date of test initiation and termination reported

MATERIALS/METHODS

2. Preparation of test diets (control/treatment) described
   - ____ Any vehicle used to dissolve or dilute test substance with the feed
   - ____ Amount of vehicle added to control diet
   - ____ Description of test diet and any other ingredients such as antibiotics, vitamins, or food additives which may have been in the feed preceding or during testing
   - ____ Type of mixer and method of mixing in the test material and vehicle
   - *____ Report data if food was analyzed for the pesticide concentration
   - ____ Method used to determine concentration levels

3. Test birds
   - ____ Mallard duck and bobwhite quail tested
   - ____ Rationale for selection of species if the species used is different than that preferred in Subdivision E

4. Breeding history
   - ____ Birds were phenotypically similar to wild counterpart, pen reared, and were in the first breeding season.
   - ____ Any observed diseases and treatments were reported

5. Description of any pretest conditioning
   - *____ Health
   - *____ Description of diet, including identification and composition
   - *____ Housing conditions described, including number of animals/cage, ambient temperature and humidity, photoperiod and lighting, and source of feed and water
   - *____ Length of observation

Criteria marked with a * are supplemental and may not be required for every study.

6. Concentration and dosage mortality data
____ Number of concentrations
____ Number of days on test material including time prior to egg laying
____ Number of animals/cage
____ Randomization plan for treatments
____ Method of identifying treatment levels
____ Length of observation period (including recovery period, if necessary)
____ Description of the steps taken to maintain the concentration(s), if the test substance is administered in the feed or water
____ Method of assigning test organisms to test and control groups

7. Experimental design
____ A minimum of 3 test groups, one control and 2 treatment groups
____ For mallards, 2 males and 5 females/pen, replicated by ≥5 pens/treatment group; or if individual pairs are used/pen, ≥12 pens/treatment group are required
____ For bobwhite quail, one male and 2 females/pen, replicated by ≥12 pens/treatment group; or if individual pairs are used/pen, >12 pens/treatment group are required

8. ____ Methods for measuring bird body weights or other physiological measures described

9. Food consumption
____ Collection methods
*____ Describe collection schedule
*____ Provisions for minimizing food spillage and preventing air contamination by volatile chemicals

10. Pen facilities described
____ Pen size and construction, including space allocations for mating and nesting; protection from weather if outdoors; and protection from injuries
____ Photoperiod and lighting, including hours/day and wattage or footcandles at bird level
____ Temperature and humidity
*____ Pen location
*____ Diagram of test layout
*____ Ventilation of pen area
____ Source and availability of water
____ Pen construction materials

Criteria marked with a * are supplemental and may not be required for every study.

11. Egg collection, storage, and incubation
    - ____ Date egg laying began reported
    - ____ Egg collecting, cleaning, and storage procedures described
    - ____ Days eggs candled for eggshell cracks, embryo viability, and embryo survival reported
    - ____ Egg rotation regime described
    - ____ Procedure used in selecting eggs for egg shell measurements reported
    - ____ Day eggs placed in hatcher and day removed reported
    - ____ Method of identifying each bird described
    - ____ Schedule and method for gross necropsies examinations, if performed
    - ____ Incubator temperature and humidity
    - ____ Hatching egg storage temperature and humidity

12. ____ Describe grouping of hatchlings in relation to treatment levels and parents

13. ____ Tissue residue data from extra pen group if the test chemical is known to bioaccumulate, if performed

14. ____ Define technical terminology used to describe signs of intoxication

DISCUSSION AND RESULTS

15. ____ A summary of reproductive data and reproductive success data.

16. Reproductive data for controls and treatment levels
    - ____ Eggs laid
    - ____ Eggs cracked
    - ____ Eggs set
    - ____ Viable embryos
    - ____ Live three-week embryos
    - ____ Normal hatchlings
    - ____ 14 day-old survivors

17. Reproductive success data for controls and treatment levels
    - ____ Eggs laid/hen in 8 weeks
    - ____ Eggs cracked of eggs laid (%)
    - ____ Viable embryos of eggs set
    - ____ Live three-week embryos of viable embryos (%)
    - ____ Normal hatchling of live three-week embryos
    - ____ 14 day-old survivors of normal hatchlings
    - ____ 14 day-old survivors/hen

Criteria marked with a * are supplemental and may not be required for every study.

18. Reproductive data for controls and treatment levels
    ____ Eggshell thickness data, including number of eggs analyzed and mean shell thickness
    ____ Weight (grams) of 14-day old survivors for each bird
    ____ Body weight and feed consumption data for each bird for duration of the study
    ____ Reproduction data for each pen, including eggs laid, eggs cracked, eggs set, viable embryos, live 3-week embryos, normal hatchlings, and egg shell thickness data
    ____ 14-day old survivors by week, for at least 8 weeks

19.*____ If any statistical differences are found discuss their biological significance

20. ____ Statistical method(s) used for analyzing data are referenced.

21. ____ Describe and discuss control bird reproduction parameters behavior, and general health which appear atypical.

22. ____ Description of nature, incidence, time of occurrence, severity, and duration of all observed toxic effects, including all morphological and physiological responses, death and any other abnormal or unusual signs and symptoms. For example, report any specific signs of intoxication associated with death and the time of onset and remission of toxic signs. Also, report recovery time for affected birds. In addition, marked observations of fecal material should be reported.

23. ____ Gross pathological changes as noted by observation or gross necropsies examination including characterization of gross lesions.

24. ____ Report repellency of the diet or lack of palatability.

25.*____ No-observed-effect level, if determined.

26. ____ Report the results of residue analysis of test diet

27.*____ Degree of bioaccumulation if this portion of the study is performed

28. The relationship between the results of the study and the test chemical described, including
    ____ Obvious problems that occurred during the study as well as the effect, if any, these problems had on the outcome of the study
    ____ Rationale for major deviations from the protocol

29.*____ Graphs, printouts and other calculations are attached to the report

Criteria marked with a * are supplemental and may not be required for every study.

71-4 Avian Reproduction Test for Waterfowl and Upland Game Birds

GUIDANCE FOR SUMMARIZING STUDIES

Items in summary should include the items discussed in Chapter 2 of this package and the specific items listed below.

GENERAL INFORMATION

1. Conclusions summarized, including date of test initiation and termination.

MATERIALS/METHODS

2. Description of test diet (control/treatment) preparation, including
   - Any vehicle used to dissolve or dilute test substance with the feed
3. Description of test birds, including
   - Species tested (common and scientific names)
   - Rationale for selection of species, if the species used is different than that preferred in Subdivision E
4. Description of breeding history, including
   - Similarity (in terms of phenotype) of birds to wild counterpart
   - Whether the birds were pen reared and in the first breeding season
5. Description of any pretest conditioning, including
   - Health
6. Description of concentration and dosage mortality data, including
   - Number of concentrations
   - Number of days on test material
   - Number of animals/cage
   - Length of observation period
7. Description of experimental design, including
   - Number of test groups, control, and treatment groups
   - For each species, number of birds (males and females)/pen, replication of pens/treatment group; or if individual pairs are used/pen, number of pens/treatment
8. Description of pen facilities, including
   - Pen size and construction, including space allocations for mating and nesting; protection from weather if outdoors; and protection from injuries

9. Description of egg collection, storage, and incubation
   - Date egg laying began
   - Method of identifying each bird

10. Tissue residue data from extra pen group if the test chemical is known to bioaccumulate, if performed

DISCUSSION AND RESULTS

11. Description of the reproductive data for controls and treatment levels, including
    - Eggs laid
    - Eggs cracked
    - Eggs set
    - Viable embryos
    - Live three-week embryos
    - Normal hatchlings
    - 14 day-old survivors

12. Description of the reproductive success data for controls and treatment levels, per dose
    - Eggs laid/hen in 8 weeks
    - Eggs cracked of eggs laid (%)
    - Viable embryos of eggs set
    - Live three-week embryos of viable embryos (%)
    - Normal hatchling of live three-week embryos
    - 14 day-old survivors of normal hatchlings
    - Mean value of 14 day-old survivors/hen

13. Description of the reproductive data for controls and treatment levels, per dose
    - Mean value of eggshell thickness (mm)
    - Mean value of weight (grams) of 14-day old survivors for each bird
    - 14-day old survivors by week, for at least 8 weeks

14. Discussion of biological significance, if any statistical differences are found, including references for statistical method(s) used for analyzing data are referenced.

15. Repellency of the diet or lack of palatability reported.

16. Determination of the no-observed-effect level.

17. Results of residue analysis of test diet reported.

18. Degree of bioaccumulation, if this portion of the study is performed.

19. Discussion relating the results of the study to test chemical, including
    - An explanation of obvious problems that occurred during the study and what effect, if any, these problems had on the outcome of the study.
    - The rationale for any major deviations from recommended protocol.

71-5 Simulated or Actual Field Testing for Birds and Mammals

ACCEPTANCE CRITERIA

Does your study meet the following acceptance criteria?

1.*____ The protocol was submitted/reviewed by the Agency.

2.*____ The following document was reviewed when registrant considered the suitability of summarizing the study and relying on it to support reregistration:

Guidance Document for conducting Terrestrial Field Studies, EPA 540/09-88-109, September 1988. NTIS No. PB89-124580.

This reference is available from the National Technical Information Service (NTIS). Orders may be placed to NTIS by telephone at (703) 487-4650 or by mail to the following address:

National Technical Information Service
ATTN: Order Desk
5285 Port Royal Road
Springfield, Virginia 22161

Criteria marked with a * are supplemental and may not be required for every study.

71-5 Simulated or Actual Field Testing for Birds and Mammals

GUIDANCE FOR SUMMARIZING STUDIES

Items in summary should include the items discussed in Chapter 2 of this package and the specific items listed below.

1. INTRODUCTION

   - Objective of Field Studies
   - General Approach
   - Sampling and Experimental Design

2. SCREENING STUDY

   - Objective and Scope
   - Geographic Area Selection
   - Study Site Selection
   - Number of Sites
   - Size of Study Sites
   - Chemical Application
   - Methods
   - Carcass Searches
   - Radio Telemetry
   - Test of Cholinesterase Inhibition
   - Residue Analysis
   - Behavioral Observations
   - Density and Diversity Estimates
   - Interpretation of Results

3. DEFINITIVE STUDY

- Objective and Scope
- Sampling and Experimental Design
- Study Area and Site Selection
- Number and Size of Sites
- Methods
- Mortality and Survival
- Mark-Recapture
- Territory Mapping Method
- Radio Telemetry
- Other Methods for Mortality and Survival
- Reproduction and Survival of Dependent Young
- Nest Monitoring
- Behavioral Observations
- Age Structure of Populations
- Ancillary Methods
- Interpretation of Results

4. LITERATURE CITED

72-1 Acute Toxicity Test for Freshwater Fish

ACCEPTANCE CRITERIA

The Agency will accept in fulfillment of this requirement a citation by the registrant of an appropriate study cited in one of the publications listed below. To be considered appropriate, a study must be conducted on the species and age of animal stipulated in the acceptance criteria, and must employ the form of chemical designated by the acceptance criteria. If a study that appears in any of the documents listed below meets those criteria, a registrant may be exempted from summarizing the study if the registrant submits a photocopy of the title page from the publication and a photocopy of the summarized study report from the publication. The publications that list studies acceptable to EPA are:

U.S. Department of the Interior, Manual of Acute Toxicity: Interpretation and Data Base for 410 Chemicals and 66 Species of Freshwater Animals; Fish and Wildlife Service, Resource Publication 160

U.S. Department of the Interior, Handbook of Toxicity of Pesticides to Wildlife; Fish and Wildlife Service, Resource Publication 153

U.S. Department of the Interior, Lethal Dietary Toxicities of Environmental Pollutants to Birds; Fish and Wildlife Service, Resource Publication 191

U.S. EPA, Acute Toxicity Handbook of Chemicals to Estuarine Organisms; Office of Pesticides and Toxic Substances; EPA/600/X-86/231; September 1986.

Does your study meet the following acceptance criteria?

GENERAL INFORMATION

1. ____ Date of test initiation and termination reported

MATERIALS/METHODS

2. Preparation of test solution (control/treatment) described
    ____ Any vehicle used to dissolve test material
    ____ If used, amount of vehicle added to control
    ____ Method used to get test material into solution was described
    ____ Water source
    ____ Water solubility of test material reported in ppm
    *____ Total amount of test material used
    *____ Temperature of water

Criteria marked with a * are supplemental and may not be required for every study.

3. Test fish

____ One of the following organisms was tested: rainbow trout, bluegill, brook trout, coho salmon, channel catfish, fathead minnow
*____ History of test organisms described (strain, diseases, and treatment)
*____ Health described including sickness, injuries, abnormalities, name of medication (if used), and pretest diet
*____ Age
____ Weight in grams (0.5 to 5) and length in mm reported

4. ____ Source/acclimation described -
Complete name and address of test fish supplier, source of food and dilution water, size of test container in liters (L), temperature, pH, dissolved oxygen, name of equipment used to measure water quality, feeding schedule, holding and acclimation period, test organisms from the same source, number of days held.

5. Composition and size of test vessels described

____ Material type
____ Volume in liters (L)
____ Depth of test solution in cm or volume of dilution water (L)

6. Test system described

____ Source of dilution water
____ If flow-through, system and flow rate/day described
____ Procedures used to prepare toxicant stock solution
____ Criteria used to determine effects

7. Test design followed

*____ Method used in assigning test organisms to test and control groups and the number of replicates used
____ Number of fish per dose level and control group (minimum 10 for static)
*____ Name of protocol followed during this test
____ Loading (weight per unit volume of water with no more than 0.8g/L for static and 1.0 g/L for flow-through)
____ 5 treatments and 1 control used
____ Length of exposure period (96-hours minimum)
____ Type of control (positive, negative, or solvent control)
____ Temperature (12±2°C for coldwater fish and 17±2°C or 22±2° C for warmwater fish)
*____ pH
*____ Lighting (time in hours and intensity - footcandles)
____ Dissolved oxygen
*____ Water hardness expressed in mg/L as $CaCO_3$
*____ Alkalinity expressed in mg/L as $CaCO_3$)
*____ Conductivity (umhos/cm)
*____ Range finding test results, concentrations, and mortality, if used

Criteria marked with a * are supplemental and may not be required for every study.

____ Water not aerated during exposure to pesticides (unless concentrations are measured)
*____ Water: physical characteristic at the end of test - depth and volume

DISCUSSION AND RESULTS

8. ____ LC50 value reported in ppm with 95% confidence limits. Raw mortality data provided.

9. ____ Any precipitation and solubility problems.

10. ____ Statistical method referenced.

11. ____ Discussion of concentration(s) producing intoxication provided.
    ____ Water: physical characteristic at end of test - temperature, pH, and dissolved oxygen
    ____ Concentration analysis (if flow through)
    *____ Fish physiology, locomotion, behavior and pathology described
    ____ Mortalities during the test described

12.*____ No-observed-effect level, if determined.

13. The relationship between the results of the study and the test chemical described, including
    ____ Obvious problems that occurred during the study as well as the effect, if any, these problems had on the outcome of the study
    ____ Rationale for minor deviations from the protocol

14.*____ Graphs, printouts and other calculations are attached to the report

Criteria marked with a * are supplemental and may not be required for every study.

72-1 Acute Toxicity Test for Freshwater Fish

GUIDANCE FOR SUMMARIZING STUDIES

Items in summary should include the items discussed in Chapter 2 of this package and the specific items listed below.

GENERAL INFORMATION

1. Conclusions summarized, including date of test initiation and termination.

MATERIALS/METHODS

2. Description of the test solution (control/treatment) preparation, including
   - Any vehicle used to dissolve test material
   - Water solubility of test material (ppm)

3. Description of test species (fish), including
   - Organism(s) tested (common and scientific names)
   - Weight (g) and length (mm)

4. Description of source/acclimation, including
   - Complete name and address of test fish supplier

5. Description of composition and size of test vessels, including
   - Material type

6. Description of test system, including
   - System and flow rate/day, if flow-through

7. Description of test design, including
   - Number of organisms/dose level and control group
   - Name of protocol followed during test
   - Loading
   - Number of treatments and control
   - Length of exposure period
   - Type of control
   - Temperature
   - pH
   - Dissolved oxygen
   - Water aeration during exposure to pesticides

DISCUSSION AND RESULTS

8. Results, including
   - Statistical method referenced
   - LC50 value (ppm) with 95% confidence limits
   - Description of any precipitation and solubility problems
   - Discussion of concentration(s) producing intoxication
   - The no-observed-effect level, if determined
   - Concentration analysis (if flow through)
   - Mortalities during the test

9. Discussion relating the results of the study to test chemical, including
   - An explanation of obvious problems that occurred during the study and what effect, if any, these problems had on the outcome of the study.
   - The rationale for any major deviations from recommended protocol.

72-2 Acute Toxicity Test for Freshwater Invertebrates

ACCEPTANCE CRITERIA

Does your study meet the following acceptance criteria?

GENERAL INFORMATION

1. ____ Date of test initiation and termination reported

MATERIALS/METHODS

2. Preparation of test solution (control/treatment) described
    - ____ Any vehicle used to dissolve test material
    - ____ If used, amount of vehicle added to control
    - ____ Method used to get test material into solution was described
    - *____ Water source
    - ____ Water solubility of test material reported in ppm
    - *____ Total amount of test material used
    - *____ Temperature of water reported

3. Test invertebrate
    - ____ One of the following organisms was tested: Daphnia magna, Daphnia pulex, mayflies, amphipods, stoneflies
    - *____ History of test organisms described (strain, diseases and treatment)
    - *____ Health described including sickness, injuries, abnormalities, name of medication (if used), pretest diet
    - ____ Daphnids were in first instar (≤ 24 hours old) and other invertebrates were in the second instar.

4. ____ Source/acclimation described - complete name and address of supplier, source of food and dilution water, size of test container in milliliters (mL), temperature, pH, dissolved oxygen, name of equipment used to measure water quality, feeding schedule, holding, acclimation period, test organisms are from same source, and number of days adults held.

5. Composition and size of test vessels described
    - ____ Material type
    - ____ Volume in liters (L) or size in centimeters (cm)
    - ____ Depth of test solution (cm) or volume of dilution water (L)

Criteria marked with a * are supplemental and may not be required for every study.

6. Test system described
    ____ Source of dilution water
    ____ If flow-through, system and flow rate/day described
    ____ Procedures used to prepare toxicant stock solution
    ____ Criteria used to determine effects

7. Test design followed
    ____ Method used in assigning test organisms to test and control groups and number of replicates used
    ____ At least 20 Daphnia per dose level and control group
    *____ Name of protocol followed during this test
    ____ 5 treatments and 1 control used
    ____ Length of exposure period (48 hours for Daphnids and 96 hours for other invertebrates)
    ____ Type of control (positive, negative, or solvent control)
    ____ Temperature (20±2°C for Daphnids, 17±2°C for amphipods and mayflies, and 12±2°C for stoneflies)
    ____ pH
    *____ Lighting (time in hours and intensity - footcandles)
    ____ Dissolved oxygen
    ____ Water hardness expressed in mg/L as $CaCO_3$
    *____ Alkalinity expressed in mg/L as $CaCO_3$
    *____ Conductivity (umhos/cm)
    *____ Range finding test results (concentrations and mortality), if conducted
    ____ Water not aerated during exposure to pesticide (unless concentrations are measured)
    *____ Water: physical characteristic at the end of test - depth and volume

DISCUSSION AND RESULTS

8. ____ LC50 or EC50 value reported in ppm with 95% confidence limits. Raw mortality data provided.

9. ____ Any precipitation and solubility problems described.

10. ____ Statistical method referenced.

11. ____ Discussion of concentration(s) producing intoxication provided
    ____ Water: physical characteristic at the end of test - temperature, pH, and dissolved oxygen
    ____ Concentration analysis (if flow through)
    ____ Invertebrate behavior described
    ____ Mortalities during test described

12.*____ No-observed-effect level, if determined

Criteria marked with a * are supplemental and may not be required for every study.

13. The relationship between the results of the study and the test chemical described, including
    ____ Obvious problems that occurred during the study as well as the effect, if any, these problems had on the outcome of the study
    ____ Rationale for minor deviations from the protocol

14.*____ Graphs, printouts and other calculations are attached to the report

Criteria marked with a * are supplemental and may not be required for every study.

72-2 Acute Toxicity Test for Freshwater Invertebrates

GUIDANCE FOR SUMMARIZING STUDIES

Items in summary should include the items discussed in Chapter 2 of this package and the specific items listed below.

GENERAL INFORMATION

1. Conclusions summarized, including date of test initiation and termination.

MATERIALS/METHODS

2. Description of the test solution (control/treatment), preparation including
   - Any vehicle used to dissolve test material
   - Water solubility of test material (ppm)

3. Description of test species, including
   - Organism(s) tested (common and scientific names)
   - Stage

4. Description of source/acclimation, including
   - Complete name and address of supplier

5. Description of composition and size of test vessels, including
   - Material type

6. Description of test system, including
   - System and flow rate/day, if flow-through

7. Description of test design, including
   - Number of organisms/dose level and control group
   - Name of protocol followed during test
   - Number of treatments and control
   - Length of exposure period
   - Type of control
   - Temperature
   - pH
   - Dissolved oxygen
   - Water aeration during exposure to pesticides

DISCUSSION AND RESULTS

8. Results, including
   - Statistical method referenced
   - LC50 or EC50 value (ppm) with 95% confidence limits
   - Description of any precipitation and solubility problems
   - Discussion of concentration(s) producing intoxication
   - The no-observed-effect level (if determined)
   - Concentration analysis (if flow through)
   - Invertebrate behavior
   - Mortalities during the test

9. Discussion relating the results of the study to test chemical, including
   - An explanation of obvious problems that occurred during the study and what effect, if any, these problems had on the outcome of the study.
   - The rationale for any major deviations from recommended protocol.

72-3 Acute Toxicity Test for Estuarine Fish

ACCEPTANCE CRITERIA

The Agency will accept in fulfillment of this requirement a citation by the registrant of an appropriate study cited in one of the publications listed below. To be considered appropriate, a study must be conducted on the species and age of animal stipulated in the acceptance criteria, and must employ the form of chemical designated by the acceptance criteria. If a study that appears in any of the documents listed below meets those criteria, a registrant may be exempted from summarizing the study if the registrant submits a photocopy of the title page from the publication and a photocopy of the summarized study report from the publication. The publications that list studies acceptable to EPA are:

U.S. Department of the Interior, Manual of Acute Toxicity: Interpretation and Data Base for 410 Chemicals and 66 Species of Freshwater Animals; Fish and Wildlife Service, Resource Publication 160

U.S. Department of the Interior, Handbook of Toxicity of Pesticides to Wildlife; Fish and Wildlife Service, Resource Publication 153

U.S. Department of the Interior, Lethal Dietary Toxicities of Environmental Pollutants to Birds; Fish and Wildlife Service, Resource Publication 191

U.S. EPA, Acute Toxicity Handbook of Chemicals to Estuarine Organisms; Office of Pesticides and Toxic Substances; EPA/600/X-86/231; September 1986.

Does your study meet the following acceptance criteria?

GENERAL INFORMATION

1. ____ Date of test initiation and termination reported

MATERIALS/METHODS

2. Preparation of test solution (control/treatment) described
   ____ Any vehicle used to dissolve test material
   ____ If used, amount of vehicle added to control
   ____ Method used to get test material into solution was described
   *____ Water source
   ____ Water solubility of test material reported in ppm
   *____ Total amount of test material used
   *____ Temperature of water reported
   *____ Salinity (o/oo)

Criteria marked with a * are supplemental and may not be required for every study.

3. Test fish
____ One of the following organisms was tested: silverside and sheepshead minnow
*____ History of test organisms described (strain, diseases and treatment)
*____ Health described (sickness; injuries; abnormalities; name of medication, if used; pretest diet, number of days brood fish were quarantined)
*____ Age, if known
____ Weight ranges from 0.5 to 5 grams and length reported (mm)

4. ____ Source/acclimation described -
complete name and address of test fish supplier, source of food and dilution water, size of test container in liters (L), temperature, pH, dissolved oxygen, name of equipment used to measure water quality, feeding schedule, holding, acclimation period, test organisms are from same source, salinity (o/oo)

5. Composition and size of test vessels described
____ Material type
____ Volume in liters (L) or size in centimeters (cm)
____ Depth of test solution in cm or volume of dilution water

6. Test system described
____ Source of dilution water
____ If flow-through, system and flow rate/day described
____ Procedures used to prepare toxicant stock solution
____ Criteria used to determine effects

7. Test design followed
____ Method used in assigning test organisms to test and control groups and number of replicates used
____ Minimum of 10 fish for static and 20 fish for flow-through per dose level and control group
*____ Name of protocol followed during this test
____ Loading (weight per unit volume of water with no more than 0.8 g/L for static and 1.0 g/L for flow-through)
____ 5 treatments and 1 control used
____ Minimum of 96 hour exposure period
____ Type of control (positive, negative, or solvent control)
____ Temperature (22±2° C)
____ pH
*____ Lighting (time in hours and intensity - footcandles)
____ Dissolved oxygen
*____ Conductivity (umhos/cm)
*____ Range finding test results (concentrations and mortality) if conducted
____ Water not aerated during exposure to pesticide (unless concentrations are measured)
*____ Water: physical characteristic at the end of test - depth and volume

Criteria marked with a * are supplemental and may not be required for every study.

DISCUSSION AND RESULTS

8. ____ LC50 value reported in ppm with 95% confidence limits. Raw mortality data provided.

9. ____ Any precipitation and solubility problems described.

10. ____ Statistical method referenced.

11. ____ Discussion of concentration(s) producing intoxication provided
    ____ Water: physical characteristic at the end of test - temperature, pH, and dissolved oxygen
    ____ Concentration analysis (if flow through)
    ____ Fish physiology, locomotion, behavior, and pathology described
    ____ Mortalities during test

12.*____ No-observed-effect level, if determined

13. The relationship between the results of the study and the test chemical described, including
    ____ Obvious problems that occurred during the study as well as the effect, if any, these problems had on the outcome of the study
    ____ Rationale for minor deviations from the protocol

14.*____ Graphs, printouts and other concentrations should be attached to the report

Criteria marked with a * are supplemental and may not be required for every study.

72-3 Acute Toxicity Test for Estuarine Fish

GUIDANCE FOR SUMMARIZING STUDIES

Items in summary should include the items discussed in Chapter 2 of this package and the specific items listed below.

GENERAL INFORMATION

1. Conclusions summarized, including date of test initiation and termination.

MATERIALS/METHODS

2. Description of the test solution (control/treatment), preparation, including
   - Any vehicle used to dissolve test material
   - Water solubility of test material (ppm)

3. Description of test species (fish), including
   - Organism(s) tested (common and scientific names)
   - Weight (g) and length (mm)

4. Description of source/acclimation, including
   - Complete name and address of test fish supplier

5. Description of composition and size of test vessels, including
   - Material type

6. Description of test system, including
   - Source of dilution water
   - System and flow rate/day, if flow-through

7. Description of test design, including
   - Number of fish for static and for flow-through/dose level and control group
   - Name of protocol followed during test
   - Loading
   - Number of treatments and control
   - Length of exposure period
   - Type of control
   - Temperature
   - pH
   - Dissolved oxygen
   - Water aeration during exposure to pesticides

DISCUSSION AND RESULTS

8. Results, including
    - Statistical methods referenced
    - LC50 value (ppm) with 95% confidence limits
    - Description of any precipitation and solubility problems
    - Discussion of concentration(s) producing intoxication
    - The no-observed-effect level if determined
    - Concentration analysis (if flow-through)
    - Fish physiology, locomotion, behavior, and pathology described
    - mortalities during test

9. Discussion relating the results of the study to test chemical, including
    - An explanation of obvious problems that occurred during the study and what effect, if any, these problems had on the outcome of the study.
    - The rationale for any major deviations from recommended protocol.

72-3(b) Acute Toxicity Test for Shrimp

ACCEPTANCE CRITERIA

Does your study meet the following acceptance criteria?

GENERAL INFORMATION

1. ____ Date of test initiation and termination reported

MATERIALS/METHODS

2. Preparation of test solution (control/treatment) described

    ____ Any vehicle used to dissolve test material
    ____ If used, amount of vehicle added to control
    ____ Method used to get test material into solution was described
    ____ Water source
    ____ Water solubility of test material reported in ppm
    *____ Total amount of test material used
    *____ Temperature
    *____ Salinity (o/oo)

3. Test shrimp

    ____ One of the following organisms was tested: white, pink, brown, grass and mysid
    *____ History of test organisms described (strain, diseases, and treatment)
    *____ Health described, including sickness, injuries, abnormalities, name of medication (if used), and pretest diet
    ____ Juvenile stage was tested, except for mysids which must be ≤ 24 hrs old
    ____ Weight measured in grams and length in mm, except for mysids

4. ____ Source/acclimation described -
Complete name and address of test shrimp supplier, source of food and dilution water, size of test container in liters (L), temperature, pH, dissolved oxygen, name of equipment used to measure water quality, feeding schedule, holding and acclimation period, test organisms from the same source, number of days held, salinity (o/oo).

5. Composition and size of test vessels described

    ____ Material type
    ____ Volume in liters (L) or size in centimeters (cm)
    ____ Depth of test solution in cm or volume of dilution water (L)

Criteria marked with a * are supplemental and may not be required for every study.

6. Test system described
    - ____ Source of dilution water
    - ____ If flow-through, system and flow rate/day described
    - ____ Procedures used to prepare toxicant stock solution
    - ____ Criteria used to determine effects

7. Test design followed
    - ____ Method used in assigning test shrimp to test and control groups and the number of replicates used
    - ____ Number of shrimp per dose level and control group (minimum 10 for static and 20 for flow-through)
    - *____ Name of protocol followed during this test
    - ____ Loading (weight per unit volume of water with no more than 0.8 g/L for static and 1.0 g/L for flow-through)
    - ____ 5 treatments and 1 control
    - ____ Length of exposure period (96-hours minimum)
    - ____ Type of control (positive, negative, or solvent control)
    - ____ Temperature (22±2° C)
    - ____ pH
    - *____ Lighting (me in hours and intensity - footcandles)
    - ____ Dissolved oxygen
    - *____ Range finding test results, concentrations, and mortality, if used
    - ____ Water not aerated during exposure to pesticides (unless concentrations are measured)
    - *____ Water: physical characteristic at the end of test - depth and volume

DISCUSSION AND RESULTS

8. ____ LC50 value reported in ppm with 95% confidence limits. Raw mortality data provided.

9. ____ Any precipitation and solubility problems.

10. ____ Statistical method referenced.

11. ____ Discussion of concentration(s) producing intoxication provided.
    - ____ Water: physical characteristic at end of test - temperature, pH, dissolved oxygen, and salinity (o/oo)
    - ____ Concentration analysis (if flow-through)
    - ____ Shrimp physiology, locomotion, behavior and pathology described
    - ____ Mortalities during the test described

12.*____ No-observed-effect level, if determined.

Criteria marked with a * are supplemental and may not be required for every study.

13. The relationship between the results of the study and the test chemical described, including
    - ____ Obvious problems that occurred during the study as well as the effect, if any, these problems had on the outcome of the study
    - ____ Rationale for minor deviations from the protocol

14.*____ Graphs, printouts and other calculations are attached to the report

Criteria marked with a * are supplemental and may not be required for every study.

72-3(b) Acute Toxicity Test for Shrimp

GUIDANCE FOR SUMMARIZING STUDIES

Items in summary should include the items discussed in Chapter 2 of this package and the specific items listed below.

GENERAL INFORMATION

1. Conclusions summarized, including date of test initiation and termination.

MATERIALS/METHODS

2. Description of the test solution (control/treatment), preparation, including
    - Any vehicle used to dissolve test material
    - Water solubility of test material (ppm)

3. Description of test species, including
    - Organism(s) tested (common and scientific names)
    - Stage
    - Weight (g) and length (mm), except for mysids

4. Description of source/acclimation, including
    - Complete name and address of test shrimp supplier
    - Holding and acclimation period

5. Description of composition and size of test vessels, including
    - Material type

6. Description of test system, including
    - Source of dilution water
    - System and flow rate/day, if flow-through

7. Description of test design, including
    - Number of shrimp/dose level and control group
    - Name of protocol followed during test
    - Loading
    - Number of treatments and control
    - Length of exposure period
    - Type of control
    - Temperature
    - pH
    - Dissolved oxygen
    - Water aeration during exposure to pesticides
    - Salinity (o/oo)

DISCUSSION AND RESULTS

8. Results, including
   - Statistical method referenced
   - LC50 value (ppm) with 95% confidence limits
   - Description of any precipitation and solubility problems
   - Discussion of concentration(s) producing intoxication
   - The no-observed-effect level if determined
   - Concentration analysis, if flow-through

9. Discussion relating the results of the study to test chemical, including
   - An explanation of obvious problems that occurred during the study and what effect, if any, these problems had on the outcome of the study.
   - The rationale for any major deviations from recommended protocol.

72-3(c) Acute Toxicity Test for 48-hour Embryo Larvae Study and 96-hour Oyster Shell Deposition Study

ACCEPTANCE CRITERIA

Does your study meet the following acceptance criteria?

GENERAL INFORMATION

1. ____ Date of test initiation and termination reported

MATERIALS/METHODS

2. Preparation of test solution (control/treatment) described
    - ____ Any vehicle used to dissolve test material
    - ____ If used, amount of vehicle added to control
    - ____ Method used to get test material into solution was described
    - ____ Water source
    - ____ Water solubility of test material reported in ppm
    - *____ Total amount of test material used
    - *____ Salinity (o/oo)

3. Test oyster
    - ____ Atlantic oyster tested
    - *____ History of test organisms described (strain, diseases, and treatment)
    - ____ Describe fertilization process and method used to collect embryos
    - ____ For the shell deposition study, oysters should be 25-50 mm in height and for the oyster embryo larvae study, embryos should be $\leq$ 1-hour old)
    - *____ List abnormalities, if any occurred

4. ____ Source/acclimation described -
Complete name and address of test species supplier, source of food and dilution water, size of test container in liters (L), temperature, pH, dissolved oxygen, name of equipment used to measure water quality, feeding schedule, holding and acclimation period, test organisms from the same source, salinity (o/oo).

5. Composition and size of test vessels described
    - ____ Material type
    - ____ Volume in liters (L)
    - ____ Depth of test solution in cm or volume of dilution water (L)

Criteria marked with a * are supplemental and may not be required for every study.

6. Test system described
    ____ Source of dilution water
    ____ If flow-through, system and flow rate/day described
    ____ Procedures used to prepare toxicant stock solution
    ____ Criteria used to determine effects

7. Test design followed for the "embryo study"
    ____ Method used in assigning test organisms to test and control groups
    ____ Number of fertilized eggs/L of test solution (20,000-30,000)
    ____ 5 treatments and 1 control used
    ____ Length of treatment period (48 hours)
    ____ Type of control (positive, negative, or solvent control)
    *____ Temperature prior to and during spawning
    ____ pH
    *____ Lighting (time in hours and intensity - footcandles and transition period between light and dark)
    ____ Dissolved oxygen
    *____ Range finding test results, if used
    ____ Water not aerated during exposure to pesticides (unless measurements are taken)
    *____ Water: physical characteristic at the end of test - depth and volume
    *____ How embryos were collected and preserved

8. Test design followed for the "shell deposition study"
    ____ Method used in assigning test organisms to test and control groups
    ____ Number of organisms per dose level (20)
    ____ 5 treatments and 1 control
    ____ Length of exposure period (96 hours)
    ____ Type of control (positive, negative, or solvent control)
    ____ pH
    *____ Lighting (time in hours and intensity - footcandles and transition period between light and dark)
    ____ Dissolved oxygen
    *____ Range finding test results, if used
    *____ Water: physical characteristic at the end of test - depth and volume
    *____ Name of protocol used during the test
    *____ How peripheral valve edge was removed
    ____ Method used to measure oyster size

DISCUSSION AND RESULTS

9. ____ EC50 value reported in ppm with 95% confidence limits. Raw mortality data provided.

10. ____ Any precipitation and solubility problems.

11. ____ Statistical method referenced.

Criteria marked with a * are supplemental and may not be required for every study.

12. ____ Discussion of concentration(s) producing intoxication provided.
    - ____ Water: physical characteristic at end of test - temperature, pH, dissolved oxygen, and salinity (o/oo)
    - ____ Number of normal developed larvae at the end of observation
    - ____ Number of deformed larvae at the end of observation
    - ____ Percent death/effects at each dose level
    - ____ Concentration analysis (if flow through)
    - ____ Length of new shell growth

13.*____ No-observed-effect level, if determined.

14. The relationship between the results of the study and the test chemical described, including
    - ____ Obvious problems that occurred during the study as well as the effect, if any, these problems had on the outcome of the study
    - ____ Rationale for minor deviations from the protocol

15.*____ Graphs, printouts and other calculations are attached to the report

Criteria marked with a * are supplemental and may not be required for every study.

72-3(c) Acute Toxicity Test for 48-hour Embryo Larvae Study and 96-hour Oyster Shell Deposition Study

GUIDANCE FOR SUMMARIZING STUDIES

Items in summary should include the items discussed in Chapter 2 of this package and the specific items listed below.

GENERAL INFORMATION

1. Conclusions summarized, including date of test initiation and termination.

MATERIALS/METHODS

2. Description of the test solution (control/treatment), preparation, including
   - Any vehicle used to dissolve test material
   - Water solubility of test material (ppm)
3. Description of test species, including
   - Organism(s) tested (common and scientific names)
   - For shell deposition study, height of oysters and for the oyster embryo larvae study, age of embryos (hours)
4. Description of source/acclimation, including
   - Complete name and address of test species supplier
5. Description of composition and size of test vessels, including
   - Material type
6. Description of test system, including
   - Source of dilution water
   - System and flow rate/day, if flow-through
7. Description of test design for the "embryo study", including
   - Number of fertilized eggs/L of test solution
   - Number of treatments and controls
   - Length of treatment period (hours)
   - Type of control
   - Name of protocol used during test
   - Dissolved oxygen
   - Water aeration during exposure to pesticides

8. Description of test design for the "shell deposition study", including
   - Number of organisms/dose level
   - Number of treatments and controls
   - Length of exposure period (hours)
   - Type of control
   - Dissolved oxygen
   - Water aeration during exposure to pesticides
   - Name of protocol used during the test

DISCUSSION AND RESULTS

9. Results, including
   - Statistical method referenced
   - EC50 value (ppm) with 95% confidence limits
   - Description of any precipitation and solubility problems
   - Discussion of concentration(s) producing intoxication
   - No-observed-effect level, if determined
   - Length of new shell growth
   - Number of normal developed larvae at the end of observation
   - Number of deformed larvae at the end of observation

10. Discussion relating the results of the study to test chemical, including
   - An explanation of obvious problems that occurred during the study and what effect, if any, these problems had on the outcome of the study.
   - The rationale for any major deviations from recommended protocol.

6. Composition and size of test vessels described
    ____ Material type
    ____ Volume in liters (L) or size in centimeters (cm)
    ____ Depth of test solution in cm or volume of dilution water (L)

7. Test system described
    ____ Source of dilution water
    ____ If flow-through, system and flow rate/day described
    ____ Procedures used to prepare toxicant stock solution
    ____ Criteria used to determine effects

8. Test design followed
    ____ Method used in assigning test organisms to test and control groups and number of replicates used
    ____ Number of eggs per dose level and control group (80)
    *____ Name of protocol followed during this test
    ____ Loading (weight per unit volume of water)
    ____ 5 treatments and 1 control used
    ____ Length of exposure period
    ____ Type of control (positive, negative, or solvent control)
    ____ Temperature
    ____ pH
    *____ Lighting (time in hours and intensity - footcandles)
    ____ Dissolved oxygen
    ____ Water hardness
    *____ Alkalinity
    *____ Conductivity (umhos/cm)
    *____ Range finding test results (concentrations and mortality) if conducted
    *____ Water: physical characteristic at the end of test - water depth and volume
    ____ Period food was withheld prior to termination
    ____ Method used to keep eggs clean described

DISCUSSION AND RESULTS

9. ____ MATC value reported in ppm. Raw data provided.

10. ____ Any precipitation and solubility problems described.

11. ____ Statistical method referenced.

12. ____ Discussion of concentration(s) producing intoxication provided.
    ____ Water: physical characteristic at the end of test - temperature, pH, and dissolved oxygen
    ____ Concentration analysis (if flow through)

Criteria marked with a * are supplemental and may not be required for every study.

72-4 Early Life Stages Test

ACCEPTANCE CRITERIA

Does your study meet the following acceptance criteria?

GENERAL INFORMATION

1. ____ Date of test initiation and termination reported

MATERIALS/METHODS

2. Preparation of test solution (control/treatment) described
    - ____ Any vehicle used to dissolve test material
    - ____ If used, amount of vehicle added to control
    - ____ Method used to get test material into solution was described
    - ____ Water source
    - ____ Water solubility of test material reported in ppm
    - *____ Total amount of test material used
    - *____ Temperature of water reported
    - *____ Salinity (o/oo), if estuarine species is tested

3. Test fish
    - ____ One of the following organisms was tested: brook trout, rainbow trout, coho salmon, chinook, bluegill, brown trout, lake trout, northern pike, fathead minnow, channel catfish, sheepshead minnow, silverside
    - *____ History of test organisms described (strain, diseases and treatment)
    - *____ Health described (sickness; injuries; abnormalities; name of medication, if used; pretest diet, number of days brood fish were quarantined)

4. Size/age/physical condition
    - *____ Age of unfertilized eggs and milt at the beginning of test
    - *____ Procedures used to strip eggs and milt described
    - *____ Procedures used in storage and handling of eggs described
    - ____ Fertilization process described

5.*____ Source/acclimation described -
Complete name and address of test fish supplier, source of food and dilution water, size of test container in milliliters (mL), temperature, pH, dissolved oxygen, name of equipment used to measure water quality, feeding schedule, holding, acclimation period, test organisms are from same source, number of days held, salinity (o/oo)

Criteria marked with a * are supplemental and may not be required for every study.

13. ____ Signs of intoxication noted.
    - ____ Number of embryos hatched per replicate reported
    - ____ Time to hatch per replicate reported
    - ____ Mortality of embryos, larvae, and juveniles per replicate reported
    - ____ Time to swim-up per replicate reported
    - ____ Measurements of growth-weight and length per replicate reported
    - ____ Fish physiology, locomotion, behavior and pathology reported
    - ____ When larvae fish released from the retaining cup, % complete or hours elapsed identified

14.*____ No-observed-effect level, if determined.

15. The relationship between the results of the study and the test chemical described, including
    - ____ Obvious problems that occurred during the study as well as the effect, if any, these problems had on the outcome of the study
    - ____ Rationale for minor deviations from the protocol

16.*____ Graphs, printouts and other calculations are attached to report

Criteria marked with a * are supplemental and may not be required for every study.

72-4 Early Life Stage Test

GUIDANCE FOR SUMMARIZING STUDIES

Items in summary should include the items discussed in Chapter 2 of this package and the specific items listed below.

GENERAL INFORMATION

1. Conclusions summarized, including date of test initiation and termination.

MATERIALS/METHODS

2. Description of the test solution (control/treatment), preparation, including
   - Any vehicle used to dissolve test material
   - Water solubility of test material (ppm)

3. Description of test species (fish), including
   - Organism(s) tested (common and scientific names)

4. Description of size/age/physical condition
   - Age of unfertilized eggs and milt at the beginning of test

5. Description of source/acclimation, including
   - Complete name and address of test fish supplier
   - Number of males and females used/batch of eggs

6. Description of composition and size of test vessels, including
   - Material type

7. Description of test system, including
   - Source of dilution water
   - System and flow rate/day, if flow-through
   - Criteria used to determine effects

8. Description of test design, including
    - Number of eggs/dose level and control group
    - Name of protocol followed during test
    - Loading
    - Number of treatments and control
    - Length of exposure period
    - Type of control
    - Temperature
    - pH
    - Lighting (time in hours and intensity - footcandles)
    - Dissolved oxygen
    - Water aeration during exposure to pesticides

DISCUSSION AND RESULTS

9. Results, including
    - Statistical method referenced
    - Number of embryos hatched/dose
    - Time to hatch/dose
    - Mortality of embryos and larvae/dose
    - Time to swim-up/dose
    - Measurements of growth-weight and length/dose
    - Percent complete or hours elapsed when larvae fish released from the retaining cup/dose
    - MATC value (ppm)
    - Description of any precipitation and solubility problems
    - Signs of intoxication
    - Determination of the no-observed-effect level
    - Concentration analysis

10. Discussion relating the results of the study to test chemical, including
    - An explanation of obvious problems that occurred during the study and what effect, if any, these problems had on the outcome of the study.
    - The rationale for any major deviations from recommended protocol.

72-4(b) Invertebrate Life-Cycle Test (Daphnia)

ACCEPTANCE CRITERIA

Does your study meet the following acceptance criteria?

GENERAL INFORMATION

1. ____ Date of test initiation and termination reported

MATERIALS/METHODS

2. Preparation of test solution (control/treatment) described
    ____ Any vehicle used to dissolve test material
    ____ If used, amount of vehicle added to control
    ____ Method used to get test material into solution was described
    *____ Water source
    ____ Water solubility of test material reported in ppm
    *____ Total amount of test material used
    *____ Temperature of water reported

3. Test Daphnia
    ____ Daphnia magna was tested
    *____ History of test organisms described (strain, diseases and treatment)
    *____ Health described (sickness; injuries; abnormalities; name of medication, if used; pretest diet, number of days brood daphnids were quarantined)

4. Size/age/physical condition
    ____ Age of initiation of test ($\leq$24 hours)
    ____ Date spawned
    *____ List any abnormalities reported

5. ____ Source/acclimation described -
Complete name and address of Daphnia supplier, source of food and dilution water, size of test container in milliliters (mL), temperature, pH, dissolved oxygen, name of equipment used to measure water quality, feeding schedule, holding, acclimation period, test organisms are from same source, number of days adults held in laboratory prior to use of offspring

6. Composition and size of test vessels described
    ____ Material type
    ____ Volume in liters (L) or size in centimeters (cm)
    ____ Depth of test solution in cm or volume of dilution water (L)

Criteria marked with a * are supplemental and may not be required for every study.

7. Test system described
    ____ Source of dilution water
    ____ If renewal, schedule described
    ____ If flow-through, system and flow rate/day described
    ____ Procedures used to prepare toxicant stock solution
    ____ Criteria used to determine effects

8. Test design followed
    ____ Method used in assigning test organisms to test and control groups and number of replicates used
    ____ Number of daphnids per dose level and control group (minimum of 22)
    *____ Name of protocol followed during this test
    ____ 5 treatments and 1 control used
    ____ Length of exposure period (21 days)
    ____ Type of control (positive, negative, or solvent control)
    ____ Temperature (22 ± 2° C)
    ____ pH
    ____ Lighting (time in hours and intensity - footcandles)
    ____ Dissolved oxygen
    ____ Water hardness
    *____ Alkalinity
    *____ Conductivity (umhos/cm)
    *____ Range finding test results (concentrations and mortality) if conducted
    *____ Water not aerated during exposure to pesticide (unless concentrations are measured)
    *____ Water: physical characteristic at the end of test - water depth and volume
    ____ Feeding regime (food, frequency, and amount)

DISCUSSION AND RESULTS

9.____ MATC value reported in ppm. Raw data provided.

10.____ Any precipitation and solubility problems described.

11.____ Statistical method referenced.

12.____ Signs of intoxication (temporal onset, duration and concentrations that showed effects) noted.
    ____ Water: physical characteristic at the end of test - temperature, pH, and dissolved oxygen
    ____ Concentration analysis (if flow through or aeration is supplied)
    ____ Survival of first generation daphnids reported
    ____ Total young produced reported
    ____ Mortality during the test reported
    ____ Success of controls - the study is rejected if ≥ 30% total mortality, ≤ 40 young were produced, or if ephippia are produced
    ____ Daphnia physiology, locomotion, behavior and pathology defined

Criteria marked with a * are supplemental and may not be required for every study.

13. ____ The no-observed-effect level and reproductive effects defined.

14. The relationship between the results of the study and the test chemical described, including
    - ____ Obvious problems that occurred during the study as well as the effect, if any, these problems had on the outcome of the study
    - ____ Rationale for major deviations from the protocol

15.*____ Graphs, printouts and other calculations are attached to the report

Criteria marked with a * are supplemental and may not be required for every study.

72-4(b) Invertebrate Life-Cycle Test (Daphnia)

GUIDANCE FOR SUMMARIZING STUDIES

Items in summary should include the items discussed in Chapter 2 of this package and the specific items listed below.

GENERAL INFORMATION

1. Conclusions summarized, including date of test initiation and termination.

MATERIALS/METHODS

2. Description of the test solution (control/treatment), preparation, including
   - Any vehicle used to dissolve test material
   - Amount of vehicle added to control, if used
   - Water solubility of test material (ppm)

3. Description of test species, including
   - Organism(s) tested (common and scientific names)

4. Description of size/age/physical condition
   - Age at initiation of test
   - Date spawned

5. Description of source/acclimation, including
   - Complete name and address of test species supplier

6. Description of composition and size of test vessels, including
   - Material type

7. Description of test system, including
   - System and flow rate/day, if flow-through

8. Description of test design, including
   - Number of organisms/dose level and control group
   - Name of protocol followed during test
   - Number of treatments and controls
   - Length of exposure period
   - Type of control
   - Temperature
   - pH
   - Dissolved oxygen
   - Water aeration during exposure to pesticides

DISCUSSION AND RESULTS

9. Results, including
    - Statistical method referenced
    - MATC value (ppm)
    - Description of any precipitation and solubility problems
    - Determination of the no-observed-effect level and reproductive effects
    - concentration analysis (if flow through)
    - Survival of first generation organisms/dose
    - Total young produced/dose
    - Length of first generation organisms/dose
    - Mortalities during test/dose
    - Success of controls

10. Discussion relating the results of the study to test chemical, including
    - An explanation of obvious problems that occurred during the study and what effect, if any, these problems had on the outcome of the study.
    - The rationale for any major deviations from recommended protocol.

72-4(c) Invertebrate Life-Cycle Test (Mysid)

ACCEPTANCE CRITERIA

Does your study meet the following acceptance criteria?

GENERAL INFORMATION

1. ____ Date of test initiation and termination reported

MATERIALS/METHODS

2. Preparation of test solution (control/treatment) described
    ____ Any vehicle used to dissolve test material
    ____ If used, amount of vehicle added to control
    ____ Method used to get test material into solution
    *____ Water source
    ____ Water solubility of test material reported in ppm
    *____ Total amount of test material used
    *____ Water temperature
    *____ Salinity (o/oo)

3. Test mysid
    ____ *Mysidopsis bahia* tested.
    *____ History of test organisms described (strain, diseases, and treatment)
    *____ Health described, including sickness, injuries, abnormalities, name of medication (if used), pretest diet, number of days brood mysid quarantined

4. Size/age/physical condition
    ____ Age of initiation of test (≤24 hours)
    ____ Date spawned
    *____ List of any abnormalities reported

5. ____ Source/acclimation described -
Complete name and address of mysid supplier, source of food and dilution water, size of test container in milliliters (mL), temperature, pH, dissolved oxygen, name of equipment used to measure water quality, feeding schedule, holding and acclimation period, test organisms from the same source, number of days adults held in laboratory prior to use of offspring

6. Composition and size of test vessels described
    ____ Material type
    ____ Volume or size in liters (L)
    ____ Depth of test solution in centimeters (cm)

Criteria marked with a * are supplemental and may not be required for every study.

7. Test system described
    ____ Source of dilution water
    ____ If renewal, schedule described
    ____ If flow-through, system and flow rate/day described
    ____ Procedures used to prepare toxicant stock solution
    ____ Criteria used to determine effects

8. Test design followed
    ____ Method used in assigning test organisms to test and control groups, and the number of replicates used
    ____ Number of mysids/dose level and control group at the start of exposure (at least 60 organisms)
    *____ Name of protocol followed during this test
    ____ 5 treatments and 1 control used
    ____ Number of pairs for treatment and control (at least 20)
    ____ Length of exposure period with a minimum of 7 days after median time of first brood release in control
    ____ Type of control (positive, negative, or solvent control)
    ____ Temperature
    ____ pH
    ____ Lighting (time in hours and intensity - footcandles)
    ____ Dissolved oxygen
    *____ Range finding test results, concentrations, and mortality, if used
    *____ Water not aerated during exposure to pesticides (unless concentrations are measured)
    *____ Water: physical characteristic at end of test - water depth and volume
    ____ Feeding regime - food, frequency, and amount
    ____ Examination of mysid physiology, locomotion, behavior, and pathology

DISCUSSION AND RESULTS

9. Test endpoints by replicate
    ____ Water: physical characteristic at end of test - temperature, pH, and dissolved oxygen
    ____ Concentration analysis (if flow through or aeration is supplied)
    ____ Survival of first generation mysids
    ____ Live young produced by each pair
    ____ Length and dry weight of surviving first generation mysids
    ____ Mortalities during the test
    ____ Success of controls; study is rejected if $\geq$30% total adult mortality between pairing and end of test and $\leq$ average 3 young produced per female or $\geq$25% mortality of females

10. ____ MATC value reported in ppm. Raw data provided.

11. ____ Any precipitation and solubility problems described.

Criteria marked with a * are supplemental and may not be required for every study.

12. ____ Statistical method referenced.

13. ____ Signs of intoxication (temporal onset, duration, and concentrations that showed effects) noted.

14. ____ The no-observed-effect level and reproductive effects defined.

15. The relationship between the results of the study and the test chemical described, including
    - ____ Obvious problems that occurred during the study as well as the effect, if any, these problems had on the outcome of the study
    - ____ Rationale for major deviations from the protocol

16.*____ Graphs, printouts and other calculations are attached

Criteria marked with a * are supplemental and may not be required for every study.

72-4(c) Invertebrate Life-Cycle Test (Mysid)

GUIDANCE FOR SUMMARIZING STUDIES

Items in summary should include the items discussed in Chapter 2 of this package and the specific items listed below.

GENERAL INFORMATION

1. Conclusions summarized, including date of test initiation and termination.

MATERIALS/METHODS

2. Description of the preparation of test solution (control/treatment), including
   - Any vehicle used to dissolve test material
   - Water source
   - Water solubility of test material (ppm)
   - Salinity (o/oo)

3. Description of test species, including
   - Organism(s) tested (common and scientific names)

4. Description of size/age/physical condition
   - Age of initiation of test

5. Description of source/acclimation, including
   - Complete name and address of test species supplier

6. Description of composition and size of test vessels, including
   - Material type

7. Description of test system, including
   - Source of dilution water
   - Schedule described, if renewal
   - System and flow rate/day, if flow-through

8. Description of test design, including
    - Number of replicates used
    - Number of organisms/dose level and control group at start of exposure
    - Name of protocol followed during test
    - Number of treatments and controls
    - Length of exposure period
    - Type of control
    - Temperature
    - pH
    - Lighting (time in hours and intensity - footcandles)
    - Dissolved oxygen
    - Water aeration during exposure to pesticides

DISCUSSION AND RESULTS

9. Description of endpoints by dose
    - Concentration analysis
    - Survival of first generation organisms
    - Mean value of live young produced by each pair
    - Mean value of length and dry weight of surviving first generation organisms
    - Mortalities during test
    - Success of controls

10. Results, including
    - Statistical method referenced
    - MATC value (ppm)
    - Description of any precipitation and solubility problems
    - Discussion of signs of intoxication (temporal onset, duration, and concentrations that showed effects)
    - Determination of the no-observed-effect level and reproductive effects

11. Discussion relating the results of the study to test chemical, including
    - An explanation of obvious problems that occurred during the study and what effect, if any, these problems had on the outcome of the study.
    - The rationale for any major deviations from recommended protocol.

72-5 Fish Life-Cycle Test

ACCEPTANCE CRITERIA

Does your study meet the following acceptance criteria?

GENERAL INFORMATION

1. ____ Date of test initiation and termination reported

MATERIALS/METHODS

2. Preparation of test solution (control/treatment) described
    ____ Any vehicle used to dissolve test material
    ____ If used, amount of vehicle added to control
    ____ Method used to get test material into solution was described
    ____ Water source
    ____ Water solubility of test material reported in ppm
    *____ Total amount of test material used
    *____ Temperature
    *____ Salinity (o/oo), if estuarine species is tested

3. Test fish
    ____ Fathead or sheepshead minnow tested
    *____ History of test organisms described (strain, diseases, and treatment)
    *____ Health described including sickness, injuries, abnormalities, name of medication (if used), pretest diet, number of days brood fish were quarantined

4. Size/age/physical condition
    ____ Age of unfertilized eggs and milt (in hours) at the beginning of test
    ____ Procedures used to strip eggs and milt described
    ____ Procedures used in storage and handling of eggs described
    ____ Fertilization process described

5. ____ Source/acclimation described -
Complete name and address of test fish/egg supplier, source of food and dilution water, size of test container [in milliliters (mL)], temperature, pH, and dissolved oxygen, and name of equipment used to measure water quality, feeding schedule, holding, and acclimation period, test organisms from the same source, number of days held, salinity (o/oo), number of males and females used per batch of eggs, percent mortality of brood fish, description of methods used initially to determine different stages of development.

Criteria marked with a * are supplemental and may not be required for every study.

6. Composition and size of test vessels described
    ____ Material type
    ____ Volume in liters (L) or size in centimeters (cm)
    ____ Depth of test solution in cm or volume of dilution water (L)

7. Test system described
    ____ Source of dilution water
    ____ If flow-through, system and flow rate/day described
    ____ Procedures used to prepare toxicant stock solution
    ____ Criteria used to determine effects

8. Test design followed
    ____ Method used in assigning test organisms to test and control groups, and the number of replicates used
    ____ Number of eggs per dose level and control group (100)
    *____ Name of protocol followed during this test
    ____ 5 treatments and 1 control
    ____ Length of exposure period
    ____ Type of control (positive, negative, or solvent control)
    ____ Temperature
    ____ pH
    *____ Lighting (time in hours and intensity - footcandles)
    ____ Dissolved oxygen
    ____ Water hardness
    *____ Alkalinity
    *____ Conductivity (umhos/cm)
    *____ Range finding test results (concentrations and mortality), if conducted
    *____ Water: physical characteristic at end of test - water depth and volume
    ____ Method used to keep eggs clean described
    ____ Period food was withheld prior to termination

DISCUSSION AND RESULTS

9. Effects on 1st and 2nd generation embryo/cup reported
    ____ Days to complete hatching
    ____ Total number of embryos hatched
    ____ Number of normal larvae hatched

10. Effects on 1st and 2nd generation larval-juvenile/replicate 4 to 8 weeks after hatching reported
    ____ Number of survivors
    ____ Number of abnormal fish
    ____ Types of abnormalities
    ____ Total length of all survivors
    ____ Weight of all survivors

Criteria marked with a * are supplemental and may not be required for every study.

11. ____ Effects on 1st generation juvenile-adults/replicate tank reported, including total length, weight, and sex of all fish (20 to 24 weeks)

12. Effects on 1st generation adult/pair reported
    ____ Total length and weight at time of pairing
    ____ Number of spawns
    ____ Number of embryos/spawn
    ____ Total length, weight, and sex of parental fish after last spawn

13. ____ MATC value reported in ppm. Raw data provided.

14. ____ Any precipitation and solubility problems described.

15. ____ Statistical method referenced.

16. ____ Discussion of concentration(s) producing intoxication provided.
    ____ Water: physical and chemical characteristic at end of test - temperature, pH, dissolved oxygen and chemical
    ____ Concentration analysis

17. ____ Signs of intoxication noted.
    ____ Fish physiology, locomotion, behavior and pathology reported

18. ____ The no-observed-effect level defined.

19. ____ Detailed record of spawning, fertility, and fecundity exists.
    ____ When larvae fish released from the retaining cup, percent complete or hours elapsed identified
    ____ Time to swim-up per replicate reported

20. The relationship between the results of the study and the test chemical described, including
    ____ Obvious problems that occurred during the study as well as the effect, if any, these problems had on the outcome of the study
    ____ Rationale for major deviations from the protocol

21.*____ Graphs, printouts and other calculations are attached to report

Criteria marked with a * are supplemental and may not be required for every study.

72-5 Fish Life-Cycle Test

GUIDANCE FOR SUMMARIZING STUDIES

Items in summary should include the items discussed in Chapter 2 of this package and the specific items listed below.

GENERAL INFORMATION

1. Conclusions summarized, including date of test initiation and termination.

MATERIALS/METHODS

2. Description of the test solution (control/treatment), preparation, including
   - Any vehicle used to dissolve test material
   - Water solubility of test material (ppm)
   - Salinity (o/oo), if estuarine species is tested

3. Description of test species (fish), including
   - Organism(s) tested (common and scientific names)

4. Description of size/age/physical condition
   - Age of unfertilized eggs and milt (in hours) at the beginning of test

5. Description of source/acclimation, including
   - Complete name and address of test fish/egg supplier
   - Source of test organisms
   - Number of males and females used/batch of eggs
   - Methods used to initially determine different stages of development

6. Description of composition and size of test vessels, including
   - Material type

7. Description of test system, including
   - Source of dilution water
   - System and flow rate/day, if flow-through

8. Description of test design, including
   - Number of replicates
   - Number of eggs/dose level and control group
   - Name of protocol followed during test
   - Number of treatments and control
   - Length of exposure period
   - Type of control
   - Temperature

- pH
- Dissolved oxygen
- Water aeration during exposure to pesticides

DISCUSSION AND RESULTS

9. Description of test design (continued)
    - When larvae fish released from the retaining cup, percent complete or hours elapsed
    - Time to swim-up/replicate

10. Description of effects on 1st and 2nd generation embryo/dose, including
    - Mean value of days to complete hatching
    - Mean value of total number of embryos hatched
    - Mean value of number of normal larvae hatched

11. Description of effects on 1st and 2nd generation larval-juvenile/dose 4 to 8 weeks after hatching, including
    - Number of survivors
    - Number of abnormal fish
    - Mean value of total length of all survivors
    - Mean value of weight of all survivors

12. Description of the effects on 1st generation juvenile-adults/dose, including total length and weight

13. Description of effects on 1st generation adult/dose
    - Mean value of total length and weight at time of pairing
    - Number of spawns
    - Number of embryos
    - Mean value of total length, weight, and sex of parental fish after last spawn

14. Results, including
    - Statistical method referenced
    - MATC value (ppm)
    - Description of any precipitation and solubility problems
    - Determination of the no-observed-effect level
    - Concentration analysis

15. Discussion relating the results of the study to test chemical, including
    - An explanation of obvious problems that occurred during the study, as well as the effect, if any, these problems had on the outcome of the study
    - The rationale for major deviations from the protocol

72-7 Simulated or Actual Field Testing for Aquatic Organisms

ACCEPTANCE CRITERIA

Generally, tests are unacceptable if conducted prior to 1986.
Does your study meet the following acceptance criteria?

BASIC CRITERIA

1. ____ The protocol was submitted/reviewed by the Agency.

2. ____ The following document was reviewed by the registrant when considering the suitability of summarizing the study and relying on it to support reregistration:

   Hazard Evaluation Division Technical Guidance Document - Aquatic Mesocosm Tests to Support Pesticide Registrations, EPA 540/09-88-035, March 1988. NTIS No. PB88-172465.

This reference is available from the National Technical Information Service (NTIS). Orders may be placed to NTIS by telephone at (703) 487-4650 or by mail to the following address:

National Technical Information Service
ATTN: Order Desk
5285 Port Royal Road
Springfield, Virginia 22161

Criteria marked with a * are supplemental and may not be required for every study.

72-7 Simulated or Actual Field Testing for Aquatic Organisms

GUIDANCE FOR SUMMARIZING STUDIES

Items in summary should include the items discussed in Chapter 2 of this package and the specific items listed below.

1. OBJECTIVES

2. PROPOSED DESIGN CRITERIA

   - Physical Description
   - Experimental design
   - Mesocosm number
   - Mesocosm size
   - Mesocosm features
   - Mesocosm biota
   - Mesocosm treatment

3. MEASURED PARAMETERS

   - Chemical/Physical Properties
   - Biological Structure
   - Residue Analysis
   - Meteorological Conditions

4. RATIONALE

5. INTERPRETATION OF RESULTS

6. LITERATURE CITED

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81-1 Acute Oral Toxicity in the Rat

ACCEPTANCE CRITERIA

Does your study meet the following acceptance criteria?

1. ____ Technical form of the active ingredient tested. (for reregistration only)
2.* ____ At least 5 young adult rats/sex/group
3. ____ Dosing, single oral may be administered over 24 hrs.
4.* ____ Vehicle control if other than water.
5. ____ Doses tested, sufficient to determine a toxicity category or a limit dose (5000 mg/kg).
6. ____ Individual observations at least once a day.
7. ____ Observation period to last at least 14 days, or until all test animals appear normal whichever is longer.
8. ____ Individual daily observations.
9.* ____ Individual body weights.
10.* ____ Gross necropsy on all animals.

Criteria marked with a * are supplemental and may not be required for every study.

81-1 Acute Oral Toxicity in the Rat

GUIDANCE FOR SUMMARIZING STUDIES

Items in summary should include the items discussed in Chapter 2 of this package and the specific items listed below.

1. The form of pesticide tested, e.g. solid, liquid, percent AI in technical, etc.
2. The number of animals/dose/sex tested.
3. Dosing route and regimen.
4. Vehicle used
5. Doses tested and results
6. Individual observations on day of dosing.
7. Individual observations on day of dosing and for at least 14 days or until all animals appear normal (whichever is longer).
8. See items 6 and 7
9. Summarization of body weights
10. Summarization of gross necropsy
11. Significance of changes from the Acceptance Criteria

Subdivision F
Guideline Ref. No. 81-2
December 24, 1989

81-2 Acute Dermal Toxicity in the Rat, Rabbit or Guinea Pig

ACCEPTANCE CRITERIA

Does your study meet the following acceptance criteria?

1. ____ Technical form of the active ingredient tested. (for reregistration only)
2.*____ At least 5 animals/sex/group
3.*____ Rats 200-300 gm, rabbits 2.0-3.0 kg or guinea pigs 350-450 gm.
4. ____ Dosing, single dermal.
5. ____ Dosing duration at least 24 hours.
6.*____ Vehicle control, only if toxicity of vehicle is unknown.
7. ____ Doses tested, sufficient to determine a toxicity category or a limit dose (2000 mg/kg).
8. ____ Application site clipped or shaved at least 24 hours before dosing
9. ____ Application site at least 10% of body surface area.
10. ____ Application site covered with a porous nonirritating cover to retain test material and to prevent ingestion.
11. ____ Individual observations at least once a day.
12. ____ Observation period to last at least 14 days, or until all test animals appear normal whichever is longer.
13. ____ Individual daily observations.
14.*____ Individual body weights.
15.*____ Gross necropsy on all animals.

Criteria marked with a * are supplemental and may not be required for every study.

81-2 Acute Dermal Toxicity in the Rat, Rabbit or Guinea Pig

GUIDANCE FOR SUMMARIZING STUDIES

Items in summary should include the items discussed in Chapter 2 of this package and the specific items listed below.

1. The form of pesticide tested, e.g., solid, liquid, percent AI in technical, etc.
2. The number of animals/sex/dose
3. Weight range of animals
4. Verification of single, dermal exposure
5. Duration of dermal exposure
6. Statement of vehicle control
7. Doses tested and results
8. Preparation of application site
9. Area of application site (percent body surface)
10. Occlusion of test material on application site
11. Individual observations on day of dosing
12. Individual observations on day of dosing and for at least 14 days or until all animals appear normal (whichever is longer)
13. See items 11 and 12
14. Summarization of body weights
15. Summarization of gross necropsy
16. Significance of changes from Acceptance Criteria

Subdivision F
Guideline Ref. No. 81-3
December 24, 1989

81-3 Acute Inhalation Toxicity in the Rat

ACCEPTANCE CRITERIA

Does your study meet the following acceptance criteria?

1. ____ Technical form of the active ingredient tested. (for reregistration only)
2. ____ Product is a gas, a solid which may produce a significant vapor hazard based on toxicity and expected use or contains particles of inhalable size for man (aerodynamic diameter 15 um or less).
3.*____ At least 5 young adult rats/sex/group
4.*____ Dosing, at least 4 hours by inhalation.
5.*____ Chamber air flow dynamic, at least 10 air changes/hour, at least 19% oxygen content.
6. ____ Chamber temperature, 22° C (±2°), relative humidity 40-60%.
7. ____ Monitor rate of air flow
8. ____ Monitor actual concentrations of test material in breathing zone.
9. ____ Monitor aerodynamic particle size for aerosols.
10. ____ Doses tested, sufficient to determine a toxicity catagory or a limit dose (5 mg/L actual concentration of respirable substance).
11. ____ Individual observations at least once a day.
12. ____ Observation period to last at least 14 days, or until all test animals appear normal whichever is longer.
13. ____ Individual daily observations.
14.*____ Individual body weights.
15.*____ Gross necropsy on all animals.

Criteria marked with a * are supplemental and may not be required for every study.

81-3 Acute Inhalation Toxicity in the Rat

GUIDANCE FOR SUMMARIZING STUDIES

Items in summary should include the items discussed in Chapter 2 of this package and the specific items listed below.

1. The form of pesticide tested, e.g., solid, liquid, percent AI in technical, etc.
2. Statement of the inhalability of test substance
3. The number of animals/sex/dose
4. Duration of inhalation exposure
5. Number of chamber air changes/hour and the percent oxygen content of chamber air
6. Ranges for chamber air temperature and relative humidity
7. Air flow rate
8. Analytical concentrations of test material in breathing zone
9. Results of aerosol particle-size determination
10. Doses tested (or limit dose of 5mg/L or highest attainable)
11. Individual observations on day of dosing
12. Individual observations on day of dosing and for at least 14 days or until all animals appear normal (whichever is longer)
13. See items 11 and 12
14. Summarization of body weights
15. Summarization of gross necropsy
16. Significance of changes from Acceptance Criteria

81-4 Primary Eye Irritation in the Rabbit

ACCEPTANCE CRITERIA

Does your study meet the following acceptance criteria?

1. ____ Technical form of the active ingredient tested. (for reregistration only)
2. ____ Study not required if material is corrosive, causes severe dermal irritation or has a pH of ≤ 2 or ≥ 11.5.
3.*____ 6 adult rabbits
4. ____ Dosing, instillation into the conjunctival sac of one eye per animal.
5.*____ Dose, 0.1 ml if a liquid; 0.1 ml or not more than 100 mg if a solid, paste or particulate substance.
6. ____ Solid or granular test material ground to a fine dust.
7. ____ Eyes not washed for at least 24 hours.
8. ____ Eyes examined and graded for irritation before dosing and at 1, 24, 48 and 72 hr, then daily until eyes are normal or 21 days (whichever is shorter).
9.*____ Individual observations for the entire day of dosing.
10.*____ Individual daily observations.

Criteria marked with a * are supplemental and may not be required for every study.

81-4 Primary Eye Irritation in the Rabbit

GUIDANCE FOR SUMMARIZING STUDIES

Items in summary should include the items discussed in Chapter 2 of this package and the specific items listed below.

1. The form of pesticide tested, e.g., solid, liquid, percent AI in technical, etc.
2. State of material is corrosive, cause severe dermal irritation or has a pH of <2 or >11.5
3. Number of adult rabbits tested
4. State method of dosing, i.e., instillation into the conjunctival sac of one eye per animal
5. Dose administered
6. Note whether solid or granular test material has been ground to a fine dust
7. State whether eyes were washed and at what time post instillation (not less than 24 hours)
8. State whether eyes were examined and graded for irritation before dosing and at what periods after dosing
9. Individual observations for entire day of dosing
10. Individual observations for entire day of dosing and individual daily observations afterwards, until eyes are normal or for 21 days
11. Significance of changes from Acceptance Criteria

81-5 Primary Dermal Irritation Study

ACCEPTANCE CRITERIA

Does your study meet the following acceptance criteria?

1. ____ Technical form of the active ingredient tested. (for reregistration only)
2. ____ Study not required if material is corrosive or has a pH of ≤ 2 or ≥ 11.5.
3.*____ 6 adult animals.
4. ____ Dosing, single dermal.
5. ____ Dosing duration 4 hours.
6. ____ Application site shaved or clipped at least 24 hour prior to dosing.
7. ____ Application site approximately 6 cm^2.
8. ____ Application site covered with a gauze patch held in place with nonirritating tape
9. ____ Material removed, washed with water, without trauma to application site
10. ____ Application site examined and graded for irritation at 1, 24, 48 and 72 hr, then daily until normal or 14 days (whichever is shorter).
11.*____ Individual observations for the entire day of dosing.
12.*____ Individual daily observations.

Criteria marked with a * are supplemental and may not be required for every study.

81-5 Primary Dermal Irritation Study

GUIDANCE FOR SUMMARIZING STUDIES

Items in summary should include the items discussed in Chapter 2 of this package and the specific items listed below.

1. The form of pesticide tested, e.g., solid, liquid, percent AI in technical, etc.
2. State if material is corrosive, has a pH <2 or >11.5, or has a dermal LD-50 <200 mg/kg
3. Number of adult animals tested
4. Amount applied
5. Duration of dermal exposure
6. Preparation of application site (shaved or clipped at specified time before dosing)
7. Area of application site
8. Method for occlusion of application site
9. Note removal of test material and if skin was washed with water
10. State times post application when site was graded for irritation
11. Individual observations for entire day of dosing.
12. Individual observations for entire day of dosing and individual daily observations thereafter
13. Significance of changes from Acceptance Criteria.

81-6 Dermal Sensitization in the Guinea Pig

ACCEPTANCE CRITERIA

Does your study meet the following acceptance criteria?

1. ____ Technical form of the active ingredient tested. (for reregistration only)
2. ____ Study not required if material is corrosive or has a pH of ≤ 2 or ≥ 11.5.
3. ____ One of the following methods is utilized;
    - ____ Freund's complete adjuvant test
    - ____ Guinea pig maximization test
    - ____ Split adjuvant technique
    - ____ Buehler test
    - ____ Open epicutaneous test
    - ____ Mauer optimization test
    - ____ Footpad technique in guinea pig
    - ____ Other test accepted by OECD (specify)________________
4. ____ Complete description of test
5.*____ Reference for test.
6. ____ Test followed essentially as described in reference document.
7.*____ Positive control included.

Criteria marked with a * are supplemental and may not be required for every study.

81-6 Dermal Sensitization in the Guinea Pig

GUIDANCE FOR SUMMARIZING STUDIES

Items in summary should include the items discussed in Chapter 2 of this package and the specific items listed below.

1. The form of pesticide tested, e.g., solid, liquid, percent AI in technical, etc.
2. State if material is corrosive or has pH <2 or >11.5).
3. State specific method utilized
4. Complete description of specific method
5. Reference for the specific method employed
6. Note adherence of the protocol to that in the reference for the specific method utilized
7. State the positive control tested
8. Significance of changes from Acceptance Criteria

81-7 Acute Neurotoxicity in the Hen

ACCEPTANCE CRITERIA

Does your study meet the following acceptance criteria?

1. ____ Study performed on an organophosphate cholinesterase inhibiting compound.
2. ____ Technical form of the active ingredient tested.
3.* ____ Positive control utilized.
4. ____ Species utilized, domestic laying hen 8-14 months of age.
5. ____ Dosing oral by gavage or capsule (dermal or inhalation may be used).
6. ____ An acute oral LD_{50} is determined.
7. ____ Dose tested equal to an acute oral LD_{50} or a limit test of 5000 mg/kg.
8.* ____ Dosed animals may be protected with atropine and/or 2-PAM.
9. ____ Sufficient test animals so that at least 6 survive.
10. ____ Negative (vehicle) control group of at least 6 hens
11.* ____ Positive control of at least 4 hens. (if used)
12. ____ Test dose repeated if no signs of delayed neurotoxicity observed by 21 days after dosing.
13. ____ Observation period 21 days after each dose.
14. ____ Individual daily observations.
15. ____ Individual body weights.
16.* ____ Individual necropsy not required.
17. ____ Histopathology performed on all animals. Tissue to be fixed *in situ* preferably using whole animal perfusion techniques. At least three sections of each of the following tissues:
    ____brain, including medulla oblongata
    ____spinal cord; upper cervical, mid-thoracic and lumbro-sacral regions
    ____tibial nerve; proximal regions and branches
    ____sciatic nerve

Criteria marked with a * are supplemental and may not be required for every study.

81-7 Acute Neurotoxicity in the Hen

GUIDANCE FOR SUMMARIZING STUDIES

Items in summary should include the items discussed in Chapter 2 of this package and the specific items listed below.

1. Note that the test material is a cholinesterase-inhibiting organophosphate
2. The form of pesticide tested, e.g., solid, liquid, percent AI in technical, etc.
3. The positive control utilized
4. Species utilized (domestic laying hen, 8-14 months of age).
5. Route of exposure
6. Results of acute oral LD-50 test
7. State dose tested (equal to either acute oral LD-50 or limit test of 5,000 mg/kg)
8. Note whether animals are protected with atropine and/or 2-PAM
9. Number of test animals
10. Size of negative (vehicle) control group
11. State use of (optional) positive control
12. Note fulfillment of requirement for repeat dosing if no signs of delayed neurotoxicity by 21 days
13. Observation period (21 days after each dose)
14. Individual daily observations
15. Summary of bodyweights
16. Individual necropsy not required
17. Histopathology performed on all animals. State tissues examined and number of sections of each. Tissues to be fixed *in situ* preferably using whole animal perfusion techniques.
18. Significance of changes from Acceptance Criteria

82-1 Subchronic Feeding in the Rodent and Nonrodent

ACCEPTANCE CRITERIA

Does your study meet the following acceptance criteria?

1. ____ Technical form of the active ingredient tested.
2. ____ At least 10 rodents or 4 nonrodents/sex/group (3 test groups and control group).
3. ____ Dosing duration daily for 90-days or 5 days/week for 13 weeks.
4. ____ Doses tested include signs of toxicity at high dose but no lethality in nonrodents or a limit dose if nontoxic (1000 mg/kg).
5. ____ Doses tested include a NOEL.
6.*____ Analysis for test material stability, homogeneity and concentration in dosing medium
7. ____ Individual daily observations.
8. ____ Individual body weights.
9. ____ Individual or cage food consumption.
10.*____ Opthalmoscopic examination (at least pretest and at term) control and high dose.
11. ____ Clinical pathology data of 12 & 13 at termination for rodents; for nonrodents at the beginning then either monthly or midway and at termination.
12. ____ Hematology.

____ Erythrocyte count
____ Hemoglobin
____ Hematocrit

____ Leucocyte count
*____ Differential count
____ Platelet count (or clotting measure)

13. ____ Clinical chemistry.

*____ Alkaline phosphatase
____ Aspartate aminotransferase
*____ Creatinine kinase
____ Alanine aminotransferase
*____ Lactic dehydrogenase
____ Glucose
____ Bilirubin
*____ Cholesterol
*____ Creatinine

____ Total Protein
____ Albumin
____ Urea nitrogen
____ Inorganic phosphate
____ Calcium
*____ Potassium
____ Sodium
*____ Chloride

14.*____ Urinalysis, only when indicated by expected or observed activity. As scheduled in 11.

____ Blood
____ Protein
____ Ketone bodies
____ Appearance
____ Glucose

____Total bilirubin
*____ Urobilirubin
____ Sediment
____ Specific gravity (osmolality)
*____ Volume

15. ____ Individual necropsy of all animals.

Criteria marked with a * are supplemental and may not be required for every study.

16. ____ Histopathology of the following tissues performed on all nonrodents and rodents, all control and high dose animals, all animals that died or were killed on study, all gross lesions on all animals, target organs on all animals and lungs, liver and kidneys on all other animals.

____ aorta
____ eyes
____ caecum
____ colon
____ duodenum
____ brain†
____ skin
____ heart
____ testes†
____ pituitary
____ ileum
____ trachea
____ gall bladder
____ jejunum
____ bone marrow
____ liver†
____ lung
____ lymph nodes
____ stomach
____ mammary gland
____ spleen
____ musculature
____ epididymis
____ adrenals
____ urinary bladder
____ accessory sex organs; uterus
____ peripheral nerve
____ kidneys†
____ esophagus
____ ovaries
____ oviduct
____ pancreas
____ rectum
____ spinal cord (3x)
____ thyroid / parathyroids
____ salivary glands
____ thymus

† organs to be weighed

Criteria marked with a * are supplemental and may not be required for every study.

82-1 Subchronic Feeding in the Rodent and Nonrodent

GUIDANCE FOR SUMMARIZING STUDIES

Items in summary should include the items discussed in Chapter 2 of this package and the specific items listed below.

1. The form of the pesticide tested
2. The number of animals/dose/sex tested
3. Dosing duration and days/week
4. Dose tested and results
5. NOELs for various parameters
6. Analysis of test material, stability, homogeneity and concentration in dosing medium
7. Individual daily observations
8. Individual body weights
9. Food consumption
10. Ophthalmoscopic exam results
11. Clinical pathology at various times tested (see items 12 and 13)
12. Hematology results at various times tested
13. Clinical chemistry results at various times tested
14. Urinalysis results at various times tested
15. Necropsy results
16. Histopathology (all nonrodents and rodents, all control and high dose animals, all animals that died or were killed on study, all gross lesions on all animals, target organs on all animals and lungs, liver and kidneys on all other animals. Provide organ weights.)
17. Significance of changes from the Acceptance Criteria

82-2 Repeated Dose Dermal Toxicity (21-day) in the Rat, Rabbit or Guinea Pig

ACCEPTANCE CRITERIA

Does your study meet the following acceptance criteria?

1. ____ Technical form of the active ingredient tested.
2. ____ At least 5 animals/sex/group (3 test groups and control group).
3. ____ Dosing duration at least 6 hour/day for 21 days or 5 days/week for 3 weeks.
4. ____ Application site at least 10% of body surface area.
5. ____ Doses tested include signs of toxicity at high dose, no or minimal dermal irritation, minimal lethality or a limit dose (1000mg/kg) if nontoxic.
6.*____ Doses tested include a NOEL.
7. ____ Individual daily observations.
8. ____ Individual body weights.
9. ____ Individual or cage food consumption.
10. ____ Clinical pathology data of 11 & 12 at termination.
11. ____ Hematology.
    ____ Erythrocyte count
    ____ Hemoglobin
    ____ Hematocrit
    ____ Leucocyte count
    *____ Differential count
    ____ Platelet count (or clotting measure)
12. ____ Clinical chemistry.
    *____ Alkaline phosphatase
    ____ Aspartate aminotransferase
    ____ Alanine aminotransferase
    *____ Creatinine kinase
    *____ Lactic dehydrogenase
    ____ Glucose
    ____ Bilirubin
    *____ Cholesterol
    *____ Creatinine
    ____ Total Protein
    ____ Albumin
    ____ Urea nitrogen
    ____ Inorganic phosphate
    ____ Calcium
    *____ Potassium
    ____ Sodium
    *____ Chloride
13.*____ Urinalysis, only when indicated by expected or observed activity. As scheduled in 10.
    ____ Blood
    ____ Protein
    ____ Ketone bodies
    ____ Appearance
    ____ Glucose
    ____ Total bilirubin
    *____ Urobilirubin
    ____ Sediment
    ____ Specific gravity (osmolality)
    *____ Volume
14. ____ Individual necropsy of all animals.
15. ____ Histopathology performed on all control and high dose animals, all animals that died or were killed on study consisting of all gross lesions on all animals, target organs on all animals (to determine a NOEL), and skin (normal and treated) lungs, liver and kidneys.

Criteria marked with a * are supplemental and may not be required for every study.

82-2 Repeated Dose Dermal Toxicity (21-day) in the Rat, Rabbit or Guinea Pig

GUIDANCE FOR SUMMARIZING STUDIES

Items in summary should include the items discussed in Chapter 2 of this package and the specific items listed below.

1. Form of pesticide tested
2. Number of animals/dose/sex
3. Duration of dosings (hours/day and days/week)
4. Area of application site (absolute and percent of body surface area)
5. Doses tested and results
6. NOELs for various parameters
7. Daily observations
8. Body weights
9. Food consumption
10. Clinical pathology at various times tested (see items 11 and 12)
11. Hematology results at various times tested
12. Clinical chemistry results at various times tested
13. Urinalysis results at various time tested
14. Necropsy results
15. Histopathology (all control and high dose animals, all animals that died or were killed on study consisting of all gross lesions on all animals, target organs on all animals and skin [normal and treated] lungs, liver and kidneys)
16. Significance of changes from the Acceptance Criteria.

82-3 Repeated Dose Dermal Toxicity (90-day) in the Rat, Rabbit or Guinea Pig

ACCEPTANCE CRITERIA

Does your study meet the following acceptance criteria?

1. ____ Technical form of the active ingredient tested.
2. ____ At least 10 animals/sex/group (3 test groups and control group).
3. ____ Dosing duration at least 6 hour/day daily for 90 days or 5 days/week for 13 weeks.
4. ____ Application site at least 10% of body surface area.
5. ____ Doses tested include signs of toxicity at high dose, no or minimal dermal irritation, minimal lethality or a limit dose (1000mg/kg) if nontoxic.
6.*____ Doses tested include a NOEL.
7. ____ Individual daily observations.
8. ____ Individual body weights.
9. ____ Individual or cage food consumption.
10.*____ Opthalmoscopic examination (at least pretest and at term) control and high dose.
11. ____ Clinical pathology data of 12 & 13 in all animals at termination.
12. ____ Hematology.
    - ____ Erythrocyte count
    - ____ Hemoglobin
    - ____ Hematocrit
    - ____ Leucocyte count
    - *____ Differential count
    - ____ Platelet count (or clotting measure)
13. ____ Clinical chemistry.
    - *____ Alkaline phosphatase
    - ____ Aspartate aminotransferase
    - ____ Alanine aminotransferase
    - *____ Creatinine kinase
    - *____ Lactic dehydrogenase
    - ____ Glucose
    - ____ Bilirubin
    - *____ Cholesterol
    - *____ Creatinine
    - ____ Total Protein
    - ____ Albumin
    - ____ Urea nitrogen
    - ____ Inorganic phosphate
    - ____ Calcium
    - *____ Potassium
    - ____ Sodium
    - *____ Chloride
14.*____ Urinalysis, only when indicated by expected or observed activity. As scheduled in 11.
    - ____ Blood
    - ____ Protein
    - ____ Ketone bodies
    - ____ Appearance
    - ____ Glucose
    - ____ Total bilirubin
    - *____ Urobilirubin
    - ____ Sediment
    - ____ Specific gravity (osmolality)
    - *____ Volume
15. ____ Individual necropsy of all animals.

Criteria marked with a * are supplemental and may not be required for every study.

16. ____ Histopathology of the following tissues performed on all nonrodents and rodents, all control and high dose animals, all animals that died or were killed on study, all gross lesions on all animals, target organs on all animals and lungs, liver and kidneys on all other animals.

____ aorta
____ eyes
____ caecum
____ colon
____ duodenum
____ brain†
____ skin
____ heart
____ testes†
____ pituitary
____ ileum
____ trachea
____ gall bladder
____ jejunum
____ bone marrow
____ liver†
____ lung
____ lymph nodes
____ stomach
____ mammary gland
____ spleen
____ musculature
____ epididymis
____ adrenals
____ urinary bladder
____ peripheral nerve
____ kidneys†
____ esophagus
____ ovaries
____ oviduct
____ pancreas
____ rectum
____ spinal cord (3x)
____ thyroid / parathyroids
____ salivary glands
____ thymus
____ accessory organs; uterus

† organs to be weighed

82-3 Repeated Dose Dermal Toxicity (90-day) in the Rat, Rabbit or Guinea Pig

GUIDANCE FOR SUMMARIZING STUDIES

Items in summary should include the items discussed in Chapter 2 of this package and the specific items listed below.

1. Form of pesticide tested
2. Number of animals/dose/sex
3. Duration of dosing (hours/day and days/week)
4. Area of application site (absolute and percent of body surface area)
5. Doses tested and results
6. NOELS for various parameters
7. Daily observations
8. Body weights
9. Food consumption
10. Ophthalmoscopic exam
11. Clinical pathology at various times tested (see items 12 and 13)
12. Hematology results at various times tested
13. Clinical chemistry results at various times tested
14. Urinalysis results at various times tested
15. Necropsy result
16. Histopathology (all control and high dose animals, all animals that died or were killed on study consisting of all gross lesions on all animals, target organs on all animals and skin [normal and treated] lungs, liver and kidneys)
17. Significant changes from the Acceptance Criteria.

82-4 Subchronic Inhalation Toxicity (90-day) in the Rat

ACCEPTANCE CRITERIA

Does your study meet the following acceptance criteria?

1. ____ Technical form of the active ingredient tested. (for reregistration only)
2. ____ Product is a gas, a solid which may produce a significant vapor hazard based on toxicity and expected use or contains particles of inhalable size for man (aerodynamic diameter 15 um or less).
3. ____ At least 10 young adult rats/sex/group
4. ____ Dosing, 6 hours per day, 5 days per week for 13 weeks.
5. ____ Food and water should be withheld during dosing.
6.*____ Chamber air flow dynamic, at least 10 air changes/hour, at least 19% oxygen content.
7. ____ Chamber temperature, 22° C (±2°), relative humidity 40-60%.
8.*____ Alternatively, oro-nasal or head only exposures may be used.
9. ____ Monitor rate of air flow,
10. ____ Monitor actual concentrations of test material in breathing zone.
11. ____ Monitor aerodynamic particle size for aerosols.
12. ____ Individual daily observations.
13. ____ Individual body weights.
14. ____ Individual or cage food consumption.
15.*____ Opthalmoscopic examination (at least pretest and at term) control and high dose.
16. ____ Clinical pathology data of 17 & 18 in all animals at termination.
17. ____ Hematology.
    ____ Erythrocyte count
    ____ Hemoglobin
    ____ Hematocrit
    ____ Leucocyte count
    *____ Differential count
    ____ Platelet count (or clotting measure)
18. ____ Clinical chemistry.
    *____ Alkaline phosphatase
    ____ Aspartate aminotransferase
    ____ Alanine aminotransferase
    *____ Creatinine kinase
    *____ Lactic dehydrogenase
    ____ Glucose
    ____ Bilirubin
    *____ Cholesterol
    *____ Creatinine
    ____ Total Protein
    ____ Albumin
    ____ Urea nitrogen
    ____ Inorganic phosphate
    ____ Calcium
    *____ Potassium
    ____ Sodium
    *____ Chloride
19.*____ Urinalysis, only when indicated by expected or observed activity. As scheduled in 16.
    ____ Blood
    ____ Protein
    ____ Ketone bodies
    ____ Appearance
    ____ Glucose
    ____ Total bilirubin
    *____ Urobilirubin
    ____ Sediment
    ____ Specific gravity (osmolality)
    *____ Volume
20. ____ Individual necropsy of all animals.

Criteria marked with a * are supplemental and may not be required for every study.

21. ____ Histopathology of the following tissues performed on all nonrodents and rodents, all control and high dose animals, all animals that died or were killed on study, all gross lesions on all animals, target organs on all animals and lungs, liver and kidneys on all other animals.

____ aorta
____ eyes
____ caecum
____ colon
____ duodenum
____ brain†
____ skin
____ heart
____ testes†
____ pituitary
____ ileum
____ trachea
____ gall bladder
____ jejunum
____ bone marrow
____ liver†
____ lung
____ lymph nodes
____ stomach
____ mammary gland
____ spleen
____ musculature
____ epididymis
____ adrenals
____ urinary bladder
____ peripheral nerve
____ kidneys†
____ esophagus
____ ovaries
____ oviduct
____ pancreas
____ rectum
____ spinal cord (3x)
____ thyroid / parathyroids
____ salivary glands
____ thymus
____ accessory sex organs; uterus

† organs to be weighed

82-4 Subchronic Inhalation Toxicity (90-day) in the Rat

GUIDANCE FOR SUMMARIZING STUDIES

Items in summary should include the items discussed in Chapter 2 of this package and the specific items listed below.

1. Form of pesticide tested
2. Description of physical state of pesticide
3. Number of animals/dose/sex
4. Duration of dosing (hours/day, days/week)
5. Access to food and water during dosing
6. Chamber air flow
7. Chamber temperature and relative humidity
8. Alternative types of inhalation exposure, it used, e.g. oro-nasal or head only
9. Rate of air flow
10. Actual concentrations of test material in breathing zone
11. Aerodynamic particle size (for aerosols)
12. Daily observations
13. Body weights
14. Food consumption
15. Ophthalmoscopic exams
16. Clinical pathology at various times tested (see items 17 and 18)
17. Hematology results at various times tested
18. Clinical chemistry results at various times tested
19. Urinalysis results at various times tested
20. Necropsy results
21. Histopathology (all nonrodents and rodents, all control and high dose animals, all animals that died or were killed on study, all gross lesions on all animals, target organs on all animals and lungs, liver and kidneys on all other animals. Provide organ weights.
22. Significance of changes from the Acceptance Criteria.

82-5 Subchronic Neurotoxicity (90-day) in the Hen

ACCEPTANCE CRITERIA

Does your study meet the following acceptance criteria?

1. ____ Study performed on an organophosphate cholinesterase inhibiting compound.
2.* ____ Technical form of the active ingredient tested.
3. ____ Positive control utilized. (recommended but optional)
4. ____ Species utilized, domestic laying hen 8-14 months of age.
5. ____ At least 10 animals/sex/group [3 test groups, a positive control (optional) and a negative (vehicle) control group].
6. ____ Dosing duration at least daily for 90 days or 5 days/week for 13 weeks.
7. ____ Dose route oral gavage or capsule. (dermal or inhalation may be appropriate)
8. ____ Doses tested include signs of toxicity at high dose, no or minimal lethality
9.* ____ Doses tested include a NOEL.
10. ____ Individual daily observations.
11. ____ Individual body weights.
12. ____ Individual or cage food consumption.
13.* ____ Individual necropsy not required.
14. ____ Histopathology performed on all animals. Tissue to be fixed *in situ* preferably using whole animal perfusion techniques. At least three sections of each of the following tissues:
    ____ brain, including medulla oblongata
    ____ spinal cord; upper cervical, mid-thoracic and lumbro-sacral regions
    ____ tibial nerve; proximal regions and branches
    ____ sciatic nerve

Criteria marked with a * are supplemental and may not be required for every study.

82-5 Subchronic Neurotoxicity (90-day) in the Hen

GUIDANCE FOR SUMMARIZING STUDIES

Items in summary should include the items discussed in Chapter 2 of this package and the specific items listed below.

1. Type of chemical structure
2. Form of pesticide tested
3. Positive control (if used)
4. Species and age
5. Number of animals/dose/sex tested
6. Dosing duration
7. Dosing route
8. Doses tested and results
9. NOELs for various parameter
10. Daily observations
11. Body weights
12. Food consumption
13. Necropsy (if done)
14. Histopathology (all animals providing a full description of perfusion and fixation techniques for the key tissues of the nervous system)
15. Significant changes from the Acceptance Criteria.

83-1 Chronic Feeding in the Rodent and Nonrodent

ACCEPTANCE CRITERIA

Does your study meet the following acceptance criteria?

1. ____ Technical form of the active ingredient tested.
2. ____ At least 20 rodents or 4 nonrodents/sex/group (3 test groups and control group).
3. ____ Dosing duration in rodents minimum 12 month nonfood use, 24 months food use; in nonrodents minimum 12 months[1].
4. ____ Doses tested include signs of toxicity at high dose but no lethality in nonrodents or a limit dose if nontoxic (1,000 mg/kg).
5. *____ Doses tested include a NOEL.
6. *____ Analysis for test material stability, homogeneity and concentration in dosing medium
7. ____ Individual daily observations.
8. ____ Individual body weights.
9. ____ Individual or cage food consumption.
10. *____ Opthalmoscopic examination (at least pertest and at term) control and high dose.
11. ____ Clinical pathology data for all nonrodents and at least 10 rodents/group consisting of 12, 13 & 14.
12. ____ Hematology at 6 month intervals consisting of at least;
    - ____ Erythrocyte count
    - ____ Hemoglobin
    - ____ Hematocrit
    - ____ Leucocyte count
    - *____ Differential count
    - ____ Platelet count (or clotting measure)
13. ____ Clinical chemistry at 6 month intervals consisting of at least;
    - *____ Alkaline phosphatase
    - ____ Aspartate aminotransferase
    - ____ Alanine aminotransferase
    - *____ Creatinine kinase
    - *____ Lactic dehydrogenase
    - ____ Glucose
    - ____ Bilirubin
    - *____ Cholesterol
    - *____ Creatinine
    - ____ Total Protein
    - ____ Albumin
    - ____ Urea nitrogen
    - ____ Inorganic phosphate
    - ____ Calcium
    - *____ Potassium
    - ____ Sodium
    - *____ Chloride
14. ____ Urinalysis at 6 month intervals consisting of at least;
    - ____ Blood
    - ____ Protein
    - ____ Ketone bodies
    - ____ Appearance
    - ____ Glucose
    - ____ Total bilirubin
    - *____ Urobilirubin
    - ____ Sediment
    - ____ Specific gravity (osmolality)
    - *____ Volume
15. ____ Individual necropsy of all animals.

Criteria marked with a * are supplemental and may not be required for every study.

16. ____ Histopathology of the following tissues performed on all nonrodents and rodents, all control and high dose animals, all animals that died or were killed on study, all gross lesions on all animals, target organs on all animals and lungs, liver and kidneys on all other animals.

____ aorta
____ eyes
____ caecum
____ colon
____ duodenum
____ brain†
____ skin
____ heart
____ testes†
____ pituitary
____ ileum
____ trachea
____ gall bladder
____ jejunum
____ bone marrow
____ liver†
____ lung
____ lymph nodes
____ stomach
____ mammary gland
____ spleen
____ musculature
____ epididymis
____ adrenals
____ urinary bladder
____ peripheral nerve
____ kidneys†
____ esophagus
____ ovaries
____ oviduct
____ pancreas
____ rectum
____ spinal cord (3x)
____ thyroid / parathyroids
____ salivary glands
____ thymus
____ accessory sex organs; uterus

† organs to be weighed

[1] In some cases, a six month study may be acceptable. Contact EPA to discuss the criteria for determining if such a study can be used to support reregistration.

Criteria marked with a * are supplemental and may not be required for every study.

83-1 Chronic Feeding in the Rodent and Nonrodent

GUIDANCE FOR SUMMARIZING STUDIES

Items in summary should include the items discussed in Chapter 2 of this package and the specific items listed below.

1. Form of pesticide tested.
2. Number of animals/dose/sex tested.
3. Dosing duration.
4. Doses tested and results.
5. NOEL for various parameters.
6. Analysis of test material, stability, homogeneity.
7. Daily observations.
8. Body weights.
9. Food consumption
10. Ophthalmoscopic examination.
11. Clinical pathology including hematology, clinical chemistry and urinalysis.
12. Necropsy results.
13. Histopathology (all interim sacrifice, all controls high dose animals, all animals that died or were killed on study, all gross lesions on all animals, target organs on all animals and lungs, liver and kidneys on all other animals).
14. Significant changes from the Acceptance Criteria.

83-2 Oncogenicity in Rats or Mice

ACCEPTANCE CRITERIA

Does your study meet the following acceptance criteria?

1. ____ Technical form of the active ingredient tested.
2. ____ At least 50 animals/sex/group (3 test groups and control group).
3. ____ Dosing duration is at least 18 months for mice and 24 months for rats.
4. ____ Number of survivors in any group does not fall below 50% at 15 months for mice, 18 months for rats or 25% at 18 months for mice, 24 months for rats.
5.‡____ Doses tested include an MTD or limit dose if nontoxic (1,000 mg/kg).
6.*____ Doses tested include a NOEL for systematic effects.
7.*____ Analysis for test material stability, homogeneity and concentration in dosing medium
8. ____ Individual daily observations.
9. ____ Individual body weights.
10. ____ Individual or cage food consumption.
11. ____ Individual necropsy of all animals.
12. ____ Blood smear from 10 animals/sex/dose at 12 and 18 months and termination. Differential count high dose and controls, all other doses if high dose shows pathology.
13. ____ Histopathology of the following tissues performed on all interim sacrifice animals, all control and high dose animals, all animals that died or were killed on study, all gross lesions on all animals, target organs on all animals and lungs, liver and kidneys on all other animals.

____ aorta
____ eyes
____ caecum
____ colon
____ duodenum
____ brain†
____ skin
____ heart
____ testes†
____ pituitary
____ ileum
____ trachea
____ gall bladder
____ jejunum
____ bone marrow
____ liver†
____ lung
____ lymph nodes
____ stomach
____ mammary gland
____ spleen
____ musculature
____ epididymis
____ adrenals
____ urinary bladder
____ peripheral nerve
____ kidneys†
____ esophagus
____ ovaries
____ oviduct
____ pancreas
____ rectum
____ spinal cord (3x)
____ thyroid / parathyroids
____ salivary glands
____ thymus
____ accessory sex organs; uterus

† organs to be weighed

‡ The position document entitled "Selection of a Maximum Tolerated Dose (MTD) in Oncogenicity Studies (EPA No. 540/09-88-003) stated EPA's criteria for determining if an oncongenicity study has been adequately performed in terms of doses tested. However OPP is also aware that older oncogenicity studies, upon initial review or re-review. may have been tested at doses lower than the predicted MTD. In the event that such testing appears to be at doses less than the predicted MTD, the Office of Pesticides Program has been reviewing

Criteria marked with a * are supplemental and may not be required for every study.

demonstrated oncogenicity in another species, nearness to the apparent MTD, genotoxic effects, structure-activity factors, absolute value of the highest dose tested and metabolic considerations.

Criteria marked with a * are supplemental and may not be required for every study.

83-2 Oncogenicity in Rats or Mice

GUIDANCE FOR SUMMARIZING STUDIES

Items in summary should include the items discussed in Chapter 2 of this package and the specific items listed below.

1. Form of pesticide tested
2. Number of animals/dose/sex
3. Duration of dosing
4. Survival rates
5. Description of effects at highest dose tested
6. NOELs for various parameters
7. Analysis of test material, stability, homogeneity, and concentration in dosing medium
8. Daily observations
9. Body weights
10. Food consumption
11. Necropsy results
12. Blood smear results
13. Histopathology (all interim sacrifice, all controls and high dose animals that died or were killed on study, all gross lesions on all animals, target organs on all animals, and lungs, liver, kidneys on all other animals.)
14. Significance of changes from the Acceptance Criteria.

83-3 Teratology Studies

ACCEPTANCE CRITERIA

Does your study meet the following acceptance criteria?

1. ____ Technical form of the active ingredient tested.
2. ____ At least 20 pregnant animals/dose group for mice, rats or hamsters are available. At least 12 pregnant animals/dose group for rabbits are available (three test groups and control group).
3. ____ At the high dose, overt maternal effects such as slight weight loss are reported (or a limit dose is given, 1,000 mg/kg).
4.* ____ At the low dose, no developmental toxicity is reported.
5. ____ Dosing duration is at least during the period of major organogenesis, but may extend up to one day prior to term.
6.* ____ Analysis for test material stability, homogeneity and concentration in dosing medium
7. ____ Individual daily observations.
8. ____ Individual body weights.
9. ____ Individual food consumption.
10. ____ Necropsy on all animals
11. ____ Individual uterine examination including number of fetal deaths, early and late resorptions and numbers of viable fetuses per sex.
12. ____ All ovaries examined to determine number of corpora lutea.
13. ____ Individual litter weights and/or individual fetal weights per sex/litter.
14. ____ Individual fetus external examination.
15. ____ Individual fetus skeletal examination for 1/3 to 1/2 of each litter for rodents and all for all rabbits.
16. ____ Individual fetus soft tissue examination.

Criteria marked with a * are supplemental and may not be required for every study.

83-3 Teratology Studies

GUIDANCE FOR SUMMARIZING STUDIES

Items in summary should include the items discussed in Chapter 2 of this package and the specific items listed below.

1. Form of pesticide tested.
2. Number of animals per dose and number of dose groups.
3. Number of litters per dose group.
4. Toxic signs in the dams of the high dose.
5. NOEL for developmental toxicity.
6. Dosing duration and dates.
7. Test material stability, homogeneity and concentration in the dosing medium.
8. Daily observations.
9. Body weight.
10. Food consumption.
11. Results of uterine examination (for fetal deaths, resorption and viable fetuses).
12. Results of ovarian examination (for corpora lutea).
13. Litter and fetal weight.
14. Results of fetal examination (external, skeletal and soft tissues).
15. Significance of changes form the Acceptance Criteria.

83-4 Reproduction

ACCEPTANCE CRITERIA

Does your study meet the following acceptance criteria?

1. ____ Technical form of the active ingredient tested.
2. ____ At least 20 males and sufficient females to yield 20 pregnant /dose group
3. ____ At least 3 dose groups and a control.
4. ____ At the high dose, parental toxicity is observed (or a limit dose is given, 1,000 mg/kg/day).
5.*____ At the low dose, no reproductive effects are observed.
6.*____ Analysis for test material stability, homogeneity and concentration in dosing medium
7. ____ P_1 animals 8 weeks old at the start of the study.
8. ____ Dosing is continuous starting with the P_1 animals until an individual animal is sacrificed.
9. ____ Mating is 1 male to 1 female.
10. ____ The mating period is not more than 3 weeks.
11. ____ At least two generations are bred.
12. ____ Individual daily observations.
13. ____ Individual body weights.
14. ____ Individual food consumption.
15. ____ Individual litter observations.
16. ____ Individual litter weights (pup weights) at birth and on days 4, 7 (optional), 14 and 21 .
17.*____ Sacrifice schedule, all mating males immediately after last mating, all breeding females immediately after weaning last litter, all animals not used for breeding immediately after weaning.
18.*____ Necropsy on all animals
19.*____ Histopathology of reproductive organs from all animals on the high dose and control P_1 and F_1 animals selected for mating. Animals from all other dosing groups if histological effects are observed at the high dose.
20.*____ Histopathology of all organs with gross lesions.

Criteria marked with a * are supplemental and may not be required for every study.

83-4 Reproduction

GUIDANCE FOR SUMMARIZING STUDIES

Items in summary should include the items discussed in Chapter 2 of this package and the specific items listed below.

1. Form of pesticide tested.
2. Number of dose groups and number of animals per group.
3. Age of the parent animals.
4. Signs of toxicity in the high dose group.
5. NOEL for reproductive toxicity.
6. Analysis of test material stability, homogeneity and concentration in dosing medium.
7. Duration of dosing.
8. Matings (number of females per a male, mating period).
9. Study duration (number of generations monitored).
10. Daily observations.
11. Body weights.
12. Food consumption.
13. Litter observations.
14. Litter weights.
15. Sacrifice schedule.
16. Necropsy.
17. Histopathology of reproductive system and all organs with gross lesions.
18. Significance of changes from the Acceptance Criteria.

Subdivision F
Guideline Ref. No. 83-5
December 24, 1989

83-5 Chronic Feeding/Oncogenicity in the Rat

ACCEPTANCE CRITERIA

Does your study meet the following acceptance criteria?

1. ____ Technical form of the active ingredient tested.
2. ____ At least 50 rats/sex/group (3 test groups and control group).
3. ____ Dosing duration is at least 24 months.
4. ____ Number of survivors in any group does not fall below 50% at 18 months or 25% at 24 months.
5.‡____ Doses tested include an MTD or limit dose if nontoxic (1000 mg/kg).
6.*____ Doses tested include a NOEL.
7.*____ Analysis for test material stability, homogeneity and concentration in dosing medium
8. ____ Individual daily observations.
9. ____ Individual body weights.
10. ____ Individual or cage food consumption.
11.*____ Opthalmoscopic examination (at least pertest and at term) control and high dose.
12. ____ Clinical pathology data for at least 10 rats/group consisting of 13, 14 & 15
13. ____ Hematology at 6 month intervals consisting of at least;
    - ____ Erythrocyte count
    - ____ Hemoglobin
    - ____ Hematocrit
    - ____ Leucocyte count
    - *____ Differential count
    - ____ Platelet count (or clotting measure)
14. ____ Clinical chemistry at 6 month intervals consisting of at least;
    - *____ Alkaline phosphatase
    - ____ Aspartate aminotransferase
    - ____ Alanine aminotransferase
    - *____ Creatinine kinase
    - *____ Lactic dehydrogenase
    - ____ Glucose
    - ____ Bilirubin
    - *____ Cholesterol
    - *____ Creatinine
    - ____ Total Protein
    - ____ Albumin
    - ____ Urea nitrogen
    - ____ Inorganic phosphate
    - ____ Calcium
    - *____ Potassium
    - ____ Sodium
    - *____ Chloride
15. ____ Urinalysis at 6 month intervals consisting of at least;
    - ____ Blood
    - ____ Protein
    - ____ Ketone bodies
    - ____ Appearance
    - ____ Glucose
    - ____ Total bilirubin
    - *____ Urobilirubin
    - ____ Sediment
    - ____ Specific gravity (osmolality)
    - *____ Volume
16. ____ Individual necropsy of all animals.

Criteria marked with a * are supplemental and may not be required for every study.

17. ____ Histopathology of the following tissues performed on all nonrodents and rodents, all control and high dose animals, all animals that died or were killed on study, all gross lesions on all animals, target organs on all animals and lungs, liver and kidneys on all other animals.

____ aorta
____ eyes
____ caecum
____ colon
____ duodenum
____ brain†
____ skin
____ heart
____ testes†
____ pituitary
____ ileum
____ trachea
____ gall bladder
____ jejunum
____ bone marrow
____ liver†
____ lung
____ lymph nodes
____ stomach
____ mammary gland
____ spleen
____ musculature
____ epididymis
____ adrenals
____ urinary bladder
____ peripheral nerve
____ kidneys†
____ esophagus
____ ovaries
____ oviduct
____ pancreas
____ rectum
____ spinal cord (3x)
____ thyroid / parathyroids
____ salivary glands
____ thymus
____ accessory sex organs; uterus

† organs to be weighed.

‡ The position document entitled "Selection of a Maximum Tolerated Dose (MTD) in Oncogenicity Studies (EPA No. 540/09-88-003) stated EPA's criteria for determining if an oncongenicity study has been adequately performed in terms of doses tested. However OPP is also aware that older oncogenicity studies, upon initial review or re-review. may have been tested at doses lower than the predicted MTD. In the event that such testing appears to be at doses less than the predicted MTD, the Office of Pesticides Program has been reviewing and considering the entire weight of the evidence to determine if retesting is necessary. Certain factors which affect the agency's decision to retest include but are not limited to the following: demonstrated oncogenicity in another species, nearness to the apparent MTD, genotoxic effects, structure-activity factors, absolute value of the highest dose tested and metabolic considerations.

Criteria marked with a * are supplemental and may not be required for every study.

83-5 Chronic Feeding/Oncogenicity in the Rat

GUIDANCE FOR SUMMARIZING STUDIES

Items in summary should include the items discussed in Chapter 2 of this package and the specific items listed below.

1. Form of pesticide tested.
2. Number of animals per dose per sex.
3. Duration of dosing.
4. Survival rate.
5. Toxic signs at the high dose.
6. Dosing regimen and NOEL for various parameters.
7. Analysis of test material stability, homogeneity and concentration in dosing medium.
8. Daily observations.
9. Body weights.
10. Food consumption.
11. Ophthalmoscopic examination.
12. Clinical pathology (including hematology, clinical chemistry, and urinalysis).
13. Necropsy results.
14. Histopathology (all interim sacrifice, all controls and high dose animals that dies or were killed on study, all gross lesions on all animals, target organs on all animals and lungs, liver and kidneys on all other animals).
15. Significance of changes from the Acceptance Criteria.

84-2 Mutagenicity Studies

ACCEPTANCE CRITERIA

Does your study meet the following acceptance criteria?

General Requirements

1. ____ Technical form of the active ingredient tested.
2. ____ Negative, solvent and/or vehicle control(s) for the test system.
3. ____ Positive control(s) for the test system.
4. ____ Fully identified test system, species, strain, source etc.
5. ____ Fully described method for maintaining test system.
6. ____ Fully described method for preparing test environment and administering test compond.
7. ____ Fully described metabolic acitvation system, if required.
8. ____ Determination of maximum and range of concentrations/doses used under test conditions.
9.*____ Criteria for determination of a positive effect.

Test Specific Requirements

Salmonella reverse mutation assay

1. ____ Minimum of four strains, TA98, TA100, TA1535 and TA1536. (alternatives need rationale)
2. ____ Strain specific positive controls.
3. ____ Highest concentration limited by toxicity, solubility or 5000 ug/plate.
4.*____ At least 5 different concentrations of test material at adequate intervals.
5.*____ A single positive response confirmed by testing over a narrow range of concentrations.
6.*____ At least three plates experimantal point.

Gene mutation in somatic cells in culture

1. ____ Highest concentration limited by toxicity (10-20% relative survival), solubility or 5000 ug/ml.
2.*____ At least 4 different concentrations of test material to yield a concentration related toxic effect.
3. ____ Determination of the number of cell cultures used.

In vitro mammalian cytogenetics

1. ____ Highest concentration limited by toxicity (e.g. reduced mitotic activity; alteration of cell cycle; cytotoxicity), solubility or 5000 ug/ml.
2.*____ Multiple concentrtions used to define the response.
3.*____ At least two independent cultures for each experimental point.
4. ____ Determination of culture harvest time.

Criteria marked with a * are supplemental and may not be required for every study.

In vivo mammalian cytogenetics - bone marrow

1. ____ At least 5 male and 5 female animals per experimental group.
2. ____ Highest dose limited by toxicity or 5000 mg/kg.
3. ____ Determination of sampling times.
   Aberrations; a) one treatment - 3 times in range of 6-48 hours after treatment adequately spaced with central sample at 24 hour (may be altered based on cell cycle time). b) repeated treatments - samples taken 6 and 24 hours after last treatment (may be altered based on cell cycle time).
   Micronucleus; Samples taken 3 times, starting not earlier than 12 hours after the last treatment and at appropriate intervals following the first sample, but not beyond 72 hours.
4. ____ Micronucleus assay, at least 1000 polychromatic erythrocytes/animal scored. Ratio of poly to normochromatic determined by counting 200-1000 erythrocytes (1000 OECD).

Rodent dominant lethal assay

1. ____ Sufficient number of dosed males to provide a minimum of 30 pregnant females per mating interval.
2. ____ Concurrent positive control or results from positive control conducted within 12 months in same laboratory with same strain.
3. ____ Highest dose produced toxicity or 5000 mg/kg.
4. ____ Sampling or exposure over entire spermatogenesis cycle of dosed males (8 weeks mice, 10 weeks rats)

Any mutagenicity test with suggestive or greater positive results/activity shall be submitted reqardless of missing essential items.

Criteria marked with a * are supplemental and may not be required for every study.

84-2 Mutagenicity Studies

GUIDANCE FOR SUMMARIZING STUDIES

Items in summary should include the items discussed in Chapter 2 of this package and the specific items listed below.

General Requirements

1. Form of pesticide tested.
2. Negative, solvent and/or vehicle control(s).
3. Positive control(s).
4. Test system (species, strain, source...etc.)
5. Methods used (for maintaining test system, preparing test environment, administrating test compound, preparation of metabolic activation system).
6. Range finding.
7. Criteria for determining positive response.

Specific Requirements

Salmonella reverse mutation

1. Strains used.
2. Positive controls.
3. Doses tested and limitations (toxicity, solubility).
4. Number of replicates.

Gene mutation in somatic cells in culture

1. Doses tested and limitations (toxicity, solubility).
2. Number of cell cultures used.

In vitro mammalian cytogenetics

1. Doses tested and limitations (toxicity, solubility).
2. Number of cultures for each experimental point.
3. Culture harvest.

In vivo mammalian cytogenetics - bone marrow

1. Number of animals per sex per dose.
2. Highest dose tested.
3. Sampling time.

Rodent dominant lethal assay

1. Number of pregnant females per mating interval.
2. Concurrent positive control.
3. Doses tested and limitations (Toxicity).
4. Sampling or exposure over entire spermatogenesis cycle.

85-1 Metabolism Studies

ACCEPTANCE CRITERIA

Does your study meet the following acceptance criteria?

1. ____ Analytically pure grade of the active ingredient.
2. ____ Isotopically labeled in the core of the molecule and/or significant portions thereof.

-OR-

3. ____ Analytical procedures sufficiently specific and sensitive to identify the test substance.
4. ____ Young adult rats. Other mammalian species may be used for specific purposes.
5. ____ Five male and five female rats for each dose, 4 if following OECD protocol.
6. ____ Two doses, the low to be without effect and the high to produce toxic or pharmacological signs but not severe effects or mortality.
7.* ____ Dosing group A, single low dose by intravenous route (not required if insoluble in water or normal saline).
8. ____ Dosing group B, single low dose by oral route.
9. ____ Dosing group C, 14 consecutive daily low dose of the unlabeled test material by oral route followed by a single low dose of the labeled test material.
10. ____ Dosing group D, single high dose by oral route.
11. ____ Collect individually all urine, feces and expired air for 7 days after labeled dose or until 90+ percent of the dose is excreted (whichever occurs first). Expired air not required if a pilot study shows no excretion in 24 hours.
12. ____ For dosing groups B, C and D, quantity of label in the following tissues and organs;

____ bone
____ brain
____ fat
____ testes
____ heart
____ kidney
____ tissues showing pathology in this or prior studies
____ liver
____ lung
____ blood
____ muscle
____ spleen
____ residual carcass

For all dosing groups:

13. ____ Quantities of label in urine, feces and expired air (if detected in preliminary study) at appropriate intervals (e.g. 4, 8, 12 and 24 hours, 1.5, 2, 3, 4, 5, 6 and 7 days.
14. ____ Qualitative analysis of urine and feces to detect metabolism and identify metabolites (pooled urine and feces by dosing group may be used).

NOTE The metabolism data requirement may be filled in part. For example performing the analysis on a single dose group can satisfy the requirement for that dose.

Criteria marked with a * are supplemental and may not be required for every study.

85-1 Metabolism Studies

GUIDANCE FOR SUMMARIZING STUDIES

Items in summary should include the items discussed in Chapter 2 of this package and the specific items listed below.

1. Form of pesticide used.
2. Radioactive label used and site of labeling.
3. Type and specificity of analytical procedures.
4. Animals species, strain and age.
5. Number of animals per sex per test group.
6. Number of doses tested.
7. Route of administration.
8. Sample collection and schedule.
9. Results of the qualitative and quantitative analysis of urine, feces, tissues, and expired air.

SUBDIVISION J

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122-1(a) Seed Germination/Seedling Emergence - Tier I

ACCEPTANCE CRITERIA

Does your study meet the following acceptance criteria?

GENERAL INFORMATION

1. ____ Date of test initiation and termination reported

MATERIALS/METHODS

2. Identification of test substance
    ____ Source, purity, identification number, percent active ingredient
    ____ Identity and composition of impurities
    ____ Water solubility of test material reported in ppm
    ____ Vapor pressure of test material

3. Preparation of test solution (control/treatment) described
    ____ Solvent used and amount used to dissolve test material
    ____ If used, amount of solvent added to control
    ____ Water source and description
    *____ Total amount of test material used
    *____ Temperature of water reported

4. Test Plants
    ____ Six dictyledoneae species from at least four families and four monocotyledoneae species from at least two families are required. Corn, soybean, and a root crop must be tested
    ____ Family, genus, species, and cultivar or variety

5. Composition and size of test vessels
    ____ Test vessels type, size, and shape
    ____ Depth of medium in relation to test vessel

6. Test System described
    ____ Criteria used to determine effects (i.e. phytotoxicity rating scale)

Criteria marked with a * are supplemental and may not be required for every study.

7. Test design followed

____ Test duration and observation periods five days for seed germination, and two weeks for seedling emergence
____ Dose rate in ppm (seed germination) and pounds of AI per acre (seedling emergence) at the maximum label rate
____ Method of introducing the test solution into the test vessels
____ Type and number of controls
____ Number of replicates (at least 3)
____ Substrate characteristics [name/description, physical and chemical properties including pH and % organic matter (substrate should contain no more than 3% organic matter)] and preparation technique
____ Method used to assign test organisms to test and control groups
____ Number of seeds planted/container (at least 10)
____ Date of planting
____ Description of growth chamber, greenhouse (include size and location), or field plot
____ Environmental conditions [thermoperiod, relative humidity, lighting regime (intensity, quality,and photoperiod), and watering regime] at the test location
____ Cultural practices
____ Method of statistical analysis
____ Identification of protocol followed (or include copy)

DISCUSSION AND RESULTS

8. ____ Phytotoxicity symptoms observed

9. ____ Percent germination and percent emergence at the conclusion of test as compared to controls

10. ____ Deviations from EPA Subdivision J Guidelines and protocol

11. ____ Conclusions reached based on the results of the study

12. The relationship between the results of the study and the test chemical described, including

____ Obvious problems that occurred during the study as well as the effect, if any, these problems had on the outcome of the study
____ Rationale for deviations from the protocol

Criteria marked with a * are supplemental and may not be required for every study.

122-1(a) Seed Germination/Seedling Emergence - Tier I

GUIDANCE FOR SUMMARIZING STUDIES

Items in summary should include the items discussed in Chapter 2 of this package and the specific items listed below.

GENERAL INFORMATION

1. Conclusions summarized, including date of test initiation and termination.

MATERIALS/METHODS

2. Description of test species, including
    - Family, genus, species, and cultivar or variety names

3. Description of test vessels, including
    - Test vessel type, size, and shape

4. Description of test system, including
    - Criteria used to determine effects (i.e phytotoxicity rating system)

5. Description of test design, including
    - Test duration and observation periods
    - Dose rate in ppm (seed germination) and pounds of AI per acre (seedling emergence)
    - Date of planting

DISCUSSION AND RESULTS

6. Phytotoxicity symptoms observed

7. Percent germination and percent emergence at the conclusion of test as compared to controls

8. Conclusions reached based on the results of the study

122-1(b) Vegetative Vigor - Tier I

ACCEPTANCE CRITERIA

Does your study meet the following acceptance criteria?

GENERAL INFORMATION

1. ____ Date of test initiation and termination reported

MATERIALS/METHODS

2. Identification of test substance
   - ____ Source, purity, identification number, percent active ingredient
   - ____ Identity and composition of impurities
   - ____ Water solubility of test material reported in ppm
   - ____ Vapor pressure of test material

3. Preparation of test solution (control/treatment) described
   - ____ Solvent used and amount used to dissolve test material
   - ____ If used, amount of solvent added to control
   - ____ Water source and description
   - *____ Total amount of test material used
   - *____ Temperature of water reported

4. Test Plants
   - ____ Six dicotyledoneae species from at least four families and four monocotyledoneae species from at least two families are required. Corn, soybean, and a root crop must be tested.
   - ____ Family, genus, species, and cultivar, or variety
   - ____ Source

5. Composition and size of test vessels
   - ____ Test vessel type, size, and shape
   - ____ Depth of medium in relation to test vessel

6. Test system described
   - ____ Criteria used to determine effects (i.e phytotoxicity rating system)

Criteria marked with a * are supplemental and may not be required for every study.

7. Test design followed
    - ____ Test duration and observation periods (at least 2-weeks with weekly observations)
    - ____ Dose rate in pounds of AI per acre at the maximum label rate
    - ____ Method of foliar application
    - ____ Type and number of controls
    - ____ Number of replicates (at least 3)
    - ____ Substrate characteristics [name/description, physical and chemical properties including pH and % organic matter (substrate should contain no more than 3% organic matter)] and preparation technique
    - ____ Method used to assign test organisms to test and control groups
    - ____ Number of plants/container (at least 5)
    - ____ Date of planting
    - ____ Description of growth chamber, greenhouse (include size and location) or field plot
    - ____ Environmental conditions [thermoperiod, relative humidity, lighting regime (intensity, quality, and photoperiod), and watering regime] at the test location
    - ____ Cultural practices
    - ____ Method of statistical analysis
    - ____ Identification of protocol followed (or include copy)

DISCUSSION AND RESULTS

8. ____ Phytotoxicity symptoms observed.

9. ____ Growth measurements taken (height and dry weight).

10. ____ Percent effect as compared to control.

11. ____ Deviations from EPA Subdivision J Guidelines and protocol.

12. ____ Conclusions reached based on the results of the study.

13. The relationship between the results of the study and the test chemical described, including
    - ____ Obvious problems that occurred during the study as well as the effect, if any, these problems had on the outcome of the study
    - ____ Rationale for deviations from the protocol

Criteria marked with a * are supplemental and may not be required for every study.

122-1(b) Vegetative Vigor - Tier I

GUIDANCE FOR SUMMARIZING STUDIES

Items in summary should include the items discussed in Chapter 2 of this package and the specific items listed below.

GENERAL INFORMATION

1. Conclusions summarized, including date of test initiation and termination.

MATERIALS/METHODS

2. Description of the test organisms, including
    - Family, genus, species, and cultivar or variety names

3. Description of the composition and size of test vessels,including
    - Test vessel type, size, and shape

4. Description of the test system, including
    - Criteria used to determine effects (i.e. phytotoxicity rating system)

5. Description of test design followed
    - Test duration and observation periods
    - Dose rate in ppm and pounds of AI per acre
    - Date of planting

DISCUSSION AND RESULTS

6. Phytotoxicity symptoms observed

7. Growth measurements taken (height and dry weight)

8. Percent effect compared to control

9. Conclusions reached based on the results of the study

122-2 Growth and Reproduction of Aquatic Plants – Tier I

ACCEPTANCE CRITERIA

Does your study meet the following acceptance criteria?

GENERAL INFORMATION

1. ____ Data of test initiation and termination reported.

MATERIALS/METHODS

2. Identification of test substance
    ____ Source, purity, identification number, percent active ingredient
    ____ Identity and composition of impurities
    ____ Water solubility of test material reported in ppm

3. Preparation of test solution (control/treatment) described
    ____ Solvent used and amount used to dissolve test material
    ____ If used, amount of solvent added to control
    ____ Water source and description
    *____ Total amount of test material used
    *____ Temperature of water reported

4. Test Plants
    ____ Green alga Selenastrum capricornutum, blue-green alga Anabaena flos-aquae, duckweed Lemna gibba, marine diatom Skeletonema costatum, and a freshwater diatom. Include culture type and strain (Type(s) tested dependent on pesticidal properties and use sites).
    ____ History of test organisms described
    ____ Source and acclimation described

5. Composition and size of test vessels described
    ____ Test vessel type, size, and shape
    ____ Ratio of test vessel size to medium

6. Test system described
    ____ Criteria used to determine effects (i.e. phytotoxicity rating system)

Criteria marked with a * are supplemental and may not be required for every study.

7. Test design followed
    - ____ Test duration and observation periods (algae tests at least 5 days with daily observations, Lemna test at least 14 days with 3 day observations)
    - ____ Method of introducing the test solution into the test vessels
    - ____ Dose rate in ppm at the maximum label rate
    - ____ Type and number of controls
    - ____ Number of replicates (at least 3)
    - ____ Substrate or media characteristics (including pH) and method of preparation of media
    - ____ Measured or nominal concentrations
    - ____ Number of plants and fronds/vessel, or cells/ml/vessel at the beginning of test
    - ____ Method used to assign test organisms to test and control groups
    - ____ Description of growth chamber
    - ____ Environmental conditions, ie. thermoperiod, relative humidity, lighting regime (intensity, quality, and photoperiod).
    - ____ Method of statistical analysis.
    - ____ Identification of protocol followed (or include copy).

DISCUSSION AND RESULTS

8. ____ Detrimental effect of treatment compared with control, reported in ppm. Raw data provided.

9. ____ Phytotoxicity symptoms observed.

10. ____ Number of plants and fronds/vessel, or cells/ml/vessel at conclusion of test as compared to the control group.

11. ____ Deviations from EPA Subdivision J Guidelines and protocol.

12. ____ Conclusions reached based on the results of the study.

13. The relationship between the results of the study and the test chemical described, including
    - ____ Obvious problems that occurred during the study as well as the effect, if any, these problems had on the outcome of the study
    - ____ Rationale for deviations from the protocol

Criteria marked with a * are supplemental and may not be required for every study.

122-2 Growth and Reproduction of Aquatic Plants – Tier I

GUIDANCE FOR SUMMARIZING STUDIES

Items in summary should include the items discussed in Chapter 2 of this package and the specific items listed below.

GENERAL INFORMATION

1. Conclusions summarized, including date of test initiation and termination.

MATERIALS/METHODS

2. Description of the test organisms, including
   - Common and scientific names of test organisms
3. Description of the test vessels, including:
   - Test vessel type, size and shape.
4. Description of the test system, including
   - Criteria used to determine effects (i.e. phytotoxicity rating system)
5. Description of the test design, including
   - Test duration and observation periods
   - Dose rate in ppm

DISCUSSION AND RESULTS

6. Detrimental effect compared to control reported in ppm
7. Phytotoxicity symptoms observed
8. Number of plants and fronds/vessel, or cells/ml/vessel at conclusion of test as compared to the control group
9. Conclusions reached based on the results of the study

123-1(a) Seed Germination/Seedling Emergence – Tier II

ACCEPTANCE CRITERIA

Does your study meet the following acceptance criteria?

GENERAL INFORMATION

1. ____ Date of test initiation and termination reported

MATERIALS/METHODS

2. Identification of test substance
   ____ Source, purity, identification number, percent active ingredient
   ____ Identity and composition of impurities
   ____ Water solubility of test material reported in ppm
   ____ Vapor pressure of test material

3. Preparation of test solution (control/treatment) described
   ____ Solvent used and amount used to dissolve test material
   ____ If used, amount of solvent added to control
   ____ Water source and description
   *____ Total amount of test material used
   *____ Temperature of water reported

4. Test Plants
   ____ Six dictyledoneae species from at least four families and four monocotyledoneae species from at least two families are required Corn, soybean, and a root crop must be tested. At a minimum, test those plant species of Tier 1 that exhibited phytotoxic effects.
   ____ Family, genus, species, and cultivar or variety
   ____ Source

5. Composition and size of test vessels
   ____ Test vessels type, size, and shape
   ____ Depth of medium in relation to test vessel

6. Test System described
   ____ Criteria used to determine effects (i.e. phytotoxicity rating system)

Criteria marked with a * are supplemental and may not be required for every study.

7. Test design followed

____ Test duration and observation periods five days for seed germination, and two weeks for seedling emergence
____ Dose rates in ppm (seed germination) and pounds of AI per acre (seedling emergence), at least five doses should be tested in a geometric progression including a no-effect level, a subtoxic level (<EC50), and a high dose less than the maximum label rate.
____ Method of introducing the test solution into the test vessels
____ Number of treatment levels (at least 5)
____ Type and number of controls
____ Number of replicates (at least 3)
____ Substrate characteristics [name/description, physical and chemical properties including pH and % organic matter (substrate should contain no more than 3% organic matter)] and preparation technique
____ Method used to assign test organisms to test and control groups
____ Number of seeds planted/container (at least 10)
____ Date of planting
____ Description of growth chamber, greenhouse (include size and location) or field plot
____ Environmental conditions [thermoperiod, relative humidity, lighting regime (intensity, quality, and photoperiod), and watering regime] at the test location
____ Cultural practices
____ Method of statistical analysis
____ Identification of protocol followed (or include copy)

DISCUSSION AND RESULTS

8. ____ Phytotoxicity symptoms observed

9. ____ Percent germination and percent emergence at the conclusion of test as compared to controls

10. ____ EC25 and EC50 values in ppm and pounds of AI per acre with 95% confidence limits.

11. ____ The no-observed-effect level

12. ____ Deviations from EPA Subdivision J Guidelines and protocol

13. ____ Discussion of concentration(s) producing phytotoxicity

14. ____ Conclusions reached based on the results of the study

15. The relationship between the results of the study and the test chemical described, including

____ Obvious problems that occurred during the study as well as the effect, if any, these problems had on the outcome of the study
____ Rationale for deviations from the protocol

Criteria marked with a * are supplemental and may not be required for every study.

123-1(a) Seed Germination/Seedling Emergence – Tier II

GUIDANCE FOR SUMMARIZING STUDIES

Items in summary should include the items discussed in Chapter 2 of this package and the specific items listed below.

GENERAL INFORMATION

1. Conclusions summarized, including date of test initiation and termination.

MATERIALS/METHODS

2. Description of test species, including
    - Family, genus, species, and cultivar or variety names

3. Description of test vessels, including
    - Test vessel type, size, and shape

4. Description of test system, including
    - Criteria used to determine effects (i.e. phytotoxicity rating system)

5. Description of test design, including
    - Test duration and observation periods
    - Dose rates in ppm (seed germination) and pounds of AI per acre (seedling emergence)
    - Number of treatment levels
    - Date of planting

DISCUSSION AND RESULTS

8. Phytotoxicity symptoms observed

9. Percent germination and percent emergence at the conclusion of test as compared to controls

10. EC25 and EC50 values in ppm and pounds of AI per acre with 95% confidence limits

11. The no-observed-effect level

12. Discussion of concentration(s) producing phytotoxicity

13. Conclusions reached based on the results of the study

123-1(b) Vegetative Vigor – Tier II

ACCEPTANCE CRITERIA

Does your study meet the following acceptance criteria?

GENERAL INFORMATION

1. ____ Date of test initiation and termination reported

MATERIALS/METHODS

2. Identification of test substance
    ____ Source, purity, identification number, percent active ingredient
    ____ Identity and compostion of impurities
    ____ Water solubility of test material reported in ppm
    ____ Vapor pressure of test material

3. Preparation of test solution (control/treatment) described
    ____ Solvent used and amount used to dissolve test material
    ____ If used, amount of solvent added to control
    ____ Water source and description
    *____ Total amount of test material used
    *____ Temperature of water reported

4. Test Plants
    ____ Six dicotyledoneae species from at least four families and four monocotyledoneae species from at least two families are required. Corn, soybean, and a root crop must be tested.
    ____ Family, genus, species, and cultivar, or variety
    ____ Source

5. Composition and size of test vessels
    ____ Test vessel type, size, and shape
    ____ Depth of medium in relation to test vessel

6. Test system described
    ____ Criteria used to determine effects (i.e. phytotoxicity rating system)

Criteria marked with a * are supplemental and may not be required for every study.

7. Test design followed
    ____ Test duration and observation periods (at least 2-weeks with weekly observations)
    ____ Dose rates in pounds of AI per acre; at least five doses should be tested in a geometric progression including a no-effect level, a subtoxic level (<EC50), and a high dose less than the maximum label rate.
    ____ Method of foliar application
    ____ Number of treatment levels (at least five)
    ____ Type and number of controls
    ____ Number of replicates (at least 3)
    ____ Substrate characteristics [name/description, physical and chemical properties including pH and % organic matter (substrate should contain no more than 3% organic matter)] and preparation technique
    ____ Method used to assign test organisms to test and control groups
    ____ Number of plants/container (at least 5)
    ____ Date of planting
    ____ Description of growth chamber, greenhouse (include size and location),or field plot
    ____ Environmental conditions [thermoperiod, relative humidity, lighting regime (intensity, quality, and photoperiod), and watering regime] at the test location
    ____ Cultural practices
    ____ Method of statistical analysis
    ____ Identification of protocol followed (or include copy)

DISCUSSION AND RESULTS

8. ____ Phytotoxicity symptoms observed.

9. ____ Growth measurements taken (height and dry weight).

10. ____ EC25 and EC50 values in ppm and pounds of AI per acre with 95% confidence limits.

11. ____ The no-observed-effect level.

12. ____ Deviations from EPA Subdivision J Guidelines and protocol.

13. ____ Discussion of concentration(s) producing phytotoxicity.

14. ____ Conclusions reached based on the results of the study.

15. The relationship between the results of the study and the test chemical described, including
    ____ Obvious problems that occurred during the study as well as the effect, if any, these problems had on the outcome of the study
    ____ Rationale for deviations from the protocol

Criteria marked with a * are supplemental and may not be required for every study.

123-1(b) Vegetative Vigor – Tier II

GUIDANCE FOR SUMMARIZING STUDIES

Items in summary should include the items discussed in Chapter 2 of this package and the specific items listed below.

GENERAL INFORMATION

1. Conclusions summarized, including date of test initiation and termination.

MATERIALS/METHODS

2. Description of the test organisms, including
   - Family, genus, species, and cultivar or variety names

3. Description of the composition and size of test vessels,including
   - Test vessel type, size, and shape

4. Description of the test system, including
   - Criteria used to determine effects (i.e. phytotoxicity rating system)

5. Description of test design followed
   - Test duration and observation periods
   - Dose rates in ppm and pounds of AI per acre
   - Number of treatment levels
   - Date of planting

DISCUSSION AND RESULTS

8. Phytotoxicity symptoms observed

9. Growth measurements taken (height and dry weight)

10. EC25 and EC50 values in ppm and pounds of AI per acre with 95% confidence limits

11. The no-observed-effect level

12. Discussion of concentration(s) producing phytotoxicity

13. Conclusions reached based on the results of the study

123-2 Growth and Reproduction of Aquatic Plants – Tier II

ACCEPTANCE CRITERIA

Does your study meet the following acceptance criteria?

GENERAL INFORMATION

1. ____ Data of test initiation and termination reported.

MATERIALS/METHODS

2. Identification of test substance
    - ____ Source, purity, identification number, percent active ingredient
    - *____ Identity and composition of impurities
    - ____ Water solubility of test material reported in ppm

3. Preparation of test solution (control/treatment) described
    - ____ Solvent used and amount used to dissolve test material
    - ____ If used, amount of solvent added to control
    - ____ Water source and description
    - *____ Total amount of test material used
    - *____ Temperature of water reported

4. Test Plants
    - ____ Green alga Selenastrum capricornutum, blue-green alga Anabaena flos-aquae, duckweed Lemna gibba, marine diatom Skeletonema costatum, and a freshwater diatom. Include culture type and strain.
    - ____ History of test organisms described
    - ____ Source and acclimation described

5. Composition and size of test vessels described
    - ____ Test vessel type, size, and shape
    - ____ Ratio of test vessel size to medium

6. Test system described
    - ____ Criteria used to determine effects (i.e. phytotoxicity rating system)

Criteria marked with a * are supplemental and may not be required for every study.

7. Test design followed
    - ____ Test duration and observation periods (algae tests at least 5 days with daily observations, Lemna test at least 14 days with 3 day observations)
    - ____ Method of introducing the test solution into the test vessels
    - ____ Dose rates in ppm
    - ____ Number of treatment levels (at least 5); in geometric progression. Doses should include a subtoxic (<EC50) and a non-toxic concentration. The highest dose should be less than the maximum label rate.
    - ____ Type and number of controls
    - ____ Number of replicates (at least 3)
    - ____ Substrate or media characteristics (including pH) and method of preparation of media
    - ____ Measured or nominal concentrations
    - ____ Number of plants and fronds/vessel, or cells/ml/vessel at the beginning of test
    - ____ Method used to assign test organisms to test and control groups
    - ____ Description of growth chamber
    - ____ Environmental conditions, ie. thermoperiod, relative humidity, lighting regime (intensity, quality, and photoperiod).
    - ____ Method of statistical analysis.
    - ____ Identification of protocol followed (or include copy).

DISCUSSION AND RESULTS

8. ____ EC50 values reported in ppm with 95% confidence limits. Raw data provided.

9. ____ The no-observed-effect level determined.

10. ____ Phytotoxicity symptoms observed.

11. ____ Number of plants and fronds/vessel, or cells/ml/vessel at conclusion of test as compared to the control group.

12. ____ Deviations from EPA Subdivision J Guidelines and protocol.

13. ____ Discussion of concentration(s) producing phytotoxicity provided.

14. ____ Conclusions reached based on the results of the study.

15. The relationship between the results of the study and the test chemical described, including
    - ____ Obvious problems that occurred during the study as well as the effect, if any, these problems had on the outcome of the study
    - ____ Rationale for deviations from the protocol

Criteria marked with a * are supplemental and may not be required for every study.

123-2 Growth and Reproduction Of Aquatic Plants – Tier II

GUIDANCE FOR SUMMARIZING STUDIES

Items in summary should include the items discussed in Chapter 2 of this package and the specific items listed below.

GENERAL INFORMATION

1. Conclusions summarized, including date of test initiation and termination.

MATERIALS/METHODS

3. Description of the test organisms, including
   - Common and scientific names of test organisms

4. Description of the composition and size of test vessels

5. Description of the test system, including
   - Criteria used to determine effects (i.e. phytotoxicity rating system)

6. Description of the test design. including
   - Test duration and observation periods
   - Dose rates in ppm
   - Number of treatment levels (at least five)

DISCUSSION AND RESULTS

8. EC50 values reported in ppm with 95% confidence limits

9. The no-observed-effect level determined

10. Phytotoxicity symptoms observed

11. Number of plants and fronds/vessel, or cells/ml/vessel at conclusion of test as compared to the control group

12. Discussion of concentration(s) producing phytotoxicity provided

13. Conclusions reached based on the results of the study

14. Discussion relating the results of the study to test chemical

124-1 Terrestrial Field Test – Tier III

ACCEPTANCE CRITERIA

Does your study meet the following acceptance criteria?

1. ____ The protocol was approved by the Agency.

2. ____ The following documents should be used for guidance in designing and conducting a field test:

Non-Target Plants: Terrestrial Field Testing, Tier 3, EPA 540/9-86-135, June 1986. NTIS No. PB 87-101697.

Pesticide Assessment Guidelines Subdivision J Hazard Evaluation: Nontarget Plants, EPA 540/09-82-020, October 1982. NTIS No, PB83-153940.

These references are available from the National Technical Information Service (NTIS). Orders may be placed to NTIS by telephone at (703) 487-4650 or by mail to the following address:

National Technical Information Service
ATTN: Order Desk
5285 Port Royal Road
Springfield, Virginia 22161

Criteria marked with a * are supplemental and may not be required for every study.

124-1 Terrestrial Field Test – Tier III

GUIDANCE FOR SUMMARIZING STUDIES

Items in summary should include the items discussed in Chapter 2 of this package and the specific items listed below.

1. INTRODUCTION

   - Objective of Field Studies
   - General Approach
   - Sampling and Experimental Design

2. STUDY

   - Objective and Scope
   - Geographic Area Selection
   - Study Site Selection
   - Number of Sites
   - Size of Study Sites
   - Chemical Application
   - Methods
   - Interpretation of Results

124-2 Aquatic Field Test – Tier III

ACCEPTANCE CRITERIA

Does your study meet the following acceptance criteria?

1. ____ The protocol was approved by the Agency.

2. ____ The following documents should be used for guidance in designing and conducting a field test:

   Non-Target Plants: Aquatic Field Testing, Tier 3, EPA 540/09-86-136, June 1986. NTIS No. PB 87-101705.

   Pesticide Assessment Guidelines Subdivision J Hazard Evaluation: Nontarget Plants, EPA 540/09-82-020, October 1982. NTIS No, PB83-153940.

These references are available from the National Technical Information Service (NTIS). Orders may be placed to NTIS by telephone at (703) 487-4650 or by mail to the following address:

National Technical Information Service
ATTN: Order Desk
5285 Port Royal Road
Springfield, Virginia 22161

Criteria marked with a * are supplemental and may not be required for every study.

124-2 Aquatic Field Test – Tier III

GUIDANCE FOR SUMMARIZING STUDIES

Items in summary should include the items discussed in Chapter 2 of this package and the specific items listed below.

1. INTRODUCTION

- Objective of Field Studies
- General Approach
- Sampling and Experimental Design

2. STUDY

- Objective and Scope
- Geographic Area Selection
- Study Site Selection
- Number of Sites
- Size of Study Sites
- Chemical Application
- Methods
- Interpretation of Results

SUBDIVISION K

132-1 Residue Dissipation Data 154
133-3, 133-4 Dermal and Inhalation Exposure Monitoring 156

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132-1 Residue Dissipation Data

ACCEPTANCE CRITERIA

Does your study meet the following acceptance criteria?

1. ____ Typical end-use product of the active ingredient tested.
2. ____ Site(s) tested representative of reasonable worst-case climatic conditions expected in intended use areas.
3. ____ End-use product applied by application method recommended for the crop. Application rate given and should be at the least dilution and highest, label permitted, application rate.
4. ____ Application(s) occurred at time of season that the end-use product is normally applied to achieve intended pest control.
5. ____ Meteorological conditions including temperature, wind speed, daily rainfall, and humidity provided for the duration of the study.
6. ____ Duplicate foliar and/or soil samples collected at each collection period.
7. ____ Sufficent collection times to establish dissipation curve. First sample time taken as soon as sprays dry or dusts settle. Short durations should exist between earlier sample intervals and may lengthen with later samples.
8. ____ Control and baseline foliar or soil samples collected.
9. ____ Residue storage stability, method efficency (residue recovery), and limit of quantification provided.
10. ____ Foliar residue data expressed as μg or mg/cm^2 leaf surface area.
11. ____ Soil residue data expressed as μg/g of fine soil material.
12. ____ Reported residue dissipation data in conjunction with toxicity data must be sufficient to support the determination of a reentry interval.

Criteria marked with a * are supplemental and may not be required for every study.

132-1 Residue Dissipation Data

GUIDANCE FOR SUMMARIZING STUDIES

Items in summary should include the items discussed in Chapter 2 of this package and the specific items listed below.

1. Form of pesticide tested.

2a. Site(s) tested and time of season of application(s).

2b. Description of why site(s) tested are representative of geographic and climatic conditions expected to yield reasonable worst case exposure.

2c. Meteorologic conditions for duration of study.

3. Product handled and applied.

    a. equipment
    b. application rates
    c. number of applications
    d. interval between applications (if answer to "c" is 2 or greater)

4. Description of collection techniques for foliar/soil samples.

5. Sample collection times.

6. QA/QC data including storage stability, method efficiency, field recovery, and limit of quantification provided.

7. Reporting of foliar and/or soil residue data corrected for field recovery (less than 100%).

133-3, 133-4 Dermal and Inhalation Exposure Monitoring

ACCEPTANCE CRITERIA

Does your study meet the following acceptance criteria?

1. ____ Typical end-use product of the active ingredient tested.
2. ____ End-use product applied at maximum allowable rate using equipment recommended for that end-use product on the crop.
3. ____ Dermal and inhalation exposure monitored by validated methodologies (i.e. patches, whole body dosimeters, personal air samplers), as appropriate.
4. ____ Study participant activity contributing to exposure and clothing should be consistent with typical accepted agricultural practices.
5. ____ Duration of sampling is sufficent to collect measurable residues but not excessive so that residue loss occurs.
6. ____ Each sampling period should use at least 10 workers.
7. ____ Dermal exposure for each body area monitored for each study participant.
8. ____ Total dermal and inhalation exposure reported for each individual and for the group as a whole, as appropriate.
9. ____ Storage stability, method efficency for each collection matrix, and the limit of quantification provided.
10. ____ Concurrent foliar residue data (μg or mg/cm^2) and soil residue data (μg/g fine soil material) collected as per Subdivision K section 132, as appropriate.
11. ____ Brief description of activities including: nature of human activity, principle source of exposure, typical environmental conditions, level of exertion and expected frequency and duration of monitored activity.

Criteria marked with a * are supplemental and may not be required for every study.

133-3, 133-4 Dermal and Inhalation Exposure Monitoring

GUIDANCE FOR SUMMARIZING STUDIES

Items in summary should include the items discussed in Chapter 2 of this package and the specific items listed below.

1. Form of pesticide tested.
2. Product handled and applied.
    a. equipment
    b. application rates
    c. number of applications
    d. interval between applications (if answer to "c" is 2 or greater)
3. a. Activity of study participants.
    b. Clothing scenario studied for all participants.
4. Duration of monitoring period.
5. Number of workers (replicates) monitored.
6. Method for monitoring dermal and/or inhalation exposure.
7. QA/QC data including storage stability, method efficiency field recovery for each collection matrix, and the limit of quantification provided.
8. Reporting of dermal (by patch location, body part and whole body) and/or inhalation exposure, corrected for field recovery (less than 100%).

SUBDIVISION L

141-1 Acute Toxicity Test for Honey Bees 160
141-2 Residual Toxicity Test for Honey Bees 163
141-5 Field Testing for Pollinators 166

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141-1 Acute Toxicity Test for Honey Bees

ACCEPTANCE CRITERIA

Does your study meet the following acceptance criteria?

GENERAL INFORMATION

1. _____ Date of test initiation and termination reported

MATERIALS/METHODS

2. Preparation of test solution (control/treatment) described
    _____ Any vehicle used to dissolve test material
    _____ If used, amount of vehicle added to control
    *_____ Method used to get test material into solution was described
    *_____ Water solubility of test material reported in ppm
    *_____ Total amount of test material used

3. Test Insects
    _____ Testing was conducted on the honey bee, Apis mellifera
    *_____ History of test organisms described (strain, diseases and treatment)
    *_____ Health described (sickness; injuries; abnormalities; name of medication, if used; pretest diet)

4. Test cages described
    _____ Size and composition of test cages

5. Test system described
    _____ Procedures used to prepare toxicant stock solution
    _____ Criteria used to determine effects

6. Test design followed
    *_____ Method used in assigning test bees to test and control groups and number of replicates used
    _____ Number of bees per treatment level and control
    _____ Number of treatment levels
    *_____ Method used to determine treatment levels
    _____ Number of bees per cage
    _____ Number and type of controls
    _____ Environmental conditions (ambient temperature, humidity)
    _____ Source and availability of food and water
    _____ Length of total observation period
    _____ Frequency of each observation

Criteria marked with a * are supplemental and may not be required for every study.

DISCUSSION AND RESULTS

7. ____ LD50 value reported in micrograms per bee with 95% confidence limits. (Graphs, printouts, and other calculations are optional). Raw mortality data provided.

8.*____ Detailed description of any unusual symptoms which occur.

9. ____ Statistical method referenced

10. The relationship between the results of the study and the test chemical described, including
    ____ Obvious problems that occurred during the study as well as the effect, if any, these problems had on the outcome of the study
    ____ Rationale for minor deviations from the protocol

Criteria marked with a * are supplemental and may not be required for every study.

141-1 Acute Toxicity Test for Honey Bees

GUIDANCE FOR SUMMARIZING STUDIES

Items in summary should include the items discussed in Chapter 2 of this package and the specific items listed below.

GENERAL INFORMATION

1. Conclusions summarized, including date of test initiation and termination.

MATERIALS/METHODS

2. Description of the test solution (control/treatment) preparation, including
   - Any vehicle used to dissolve test material
   - Amount of vehicle added to control, if used

3. Description of the test insects, including
   - Common and scientific names

4. Description of the test cages, including

5. Description of the test system, including
   - Criteria used to determine effects

6. Description of the test design, including
   - Number of bees per treatment level and control
   - Number of treatment levels
   - Number of bees per cage
   - Number and type of controls

DISCUSSION AND RESULTS

7. LD50 value reported in micrograms per bee with 95% confidence limits. (Graphs, printouts, and other calculations should be attached to report). Raw mortality data provided.

141-2 Residual Toxicity Test for Honey Bees

ACCEPTANCE CRITERIA

Does your study meet the following acceptance criteria?

GENERAL INFORMATION

1. ____ Dates of test initiation and termination reported

MATERIALS/METHODS

2. Preparation of test solution (control/treatment) described
   ____ Any vehicle used to dissolve test material
   ____ If used, any vehicle added to control
   ____ Amount of test material used in pounds active ingredient per acre

3. Test Insects
   ____ Testing was conducted on the honey bee, Apis mellifera
   *____ History of test organisms described (strain, diseases and treatment)
   *____ Health described (sickness; injuries; abnormalities; name of medication, if used; pretest diet)

4. Test cages described
   ____ Size and composition of test cages

5. Test system described
   ____ Procedures used to prepare toxicant solution
   ____ Criteria used to determine effects

6. Test design followed
   *____ Method used in assigning test bees to test and control groups and number of replicates used
   ____ Number of bees per treatment level and control
   ____ Number of treatment levels
   *____ Basis for selection of treatment levels
   ____ Number of bees per cage
   ____ Number and type of controls
   ____ Method of application to crop
   ____ Name of crop treated

Criteria marked with a * are supplemental and may not be required for every study.

____ Method used to harvest treated foliage
____ Amount of treated foliage per cage
____ Environmental conditions
____ Source and availability of food and water
____ Length of total observation period
____ Frequency of observations

DISCUSSION AND RESULTS

7. ____Percent mortality of test bees reported at each treatment level and time interval. (Graphs, printouts, and other calculations are optional). Raw mortality data provided.

8. ____Detailed description of any unusual symptoms which occur.

9. The relationship between the results of the study and the test chemical described, including

____ Obvious problems that occurred during the study as well as the effect, if any, these problems had on the outcome of the study
____ Rationale for minor deviations from the protocol

Criteria marked with a * are supplemental and may not be required for every study.

141-2 Residual Toxicity Test for Honey Bees

GUIDANCE FOR SUMMARIZING STUDIES

Items in summary should include the items discussed in Chapter 2 of this package and the specific items listed below.

GENERAL INFORMATION

1. Conclusions summarized, including date of test initiation and termination.

MATERIALS/METHODS

2. Description of the preparation of the test solution (control/treatment), including
    - Test material used in pounds active ingredient per acre

3. Description of the test insects, including
    - Common and scientific names

4. Description of the test cages, including
    - Size and composition of test cages

5. Description of the test system, including
    - Criteria used to determine effects

6. Description of the test design, including
    - Number of bees per treatment level and control
    - Number of treatment levels
    - Number of bees per cage
    - Number and type of controls
    - Method of application to crop
    - Name of crop treated

DISCUSSION AND RESULTS

7. Percent mortality of test bees reported at each treatment level and time interval. (Graphs, printouts, and other calculation should be attached to report). Raw mortality data provided.

141-5 Field Testing for Pollinators

ACCEPTANCE CRITERIA

Does your study meet the following acceptance criteria?

GENERAL INFORMATION

1. ____ Dates of test initiation and termination reported

MATERIALS/METHODS

2. Preparation of test solution (control/treatment) described
    ____ Any vehicle used to dissolve or dilute the test substance
    ____ Description of preparation methods

3. Test Insects
    ____ Identify test insect to species
    ____ Identify source of supply of test bees
    *____ History of test organisms described (strain, diseases and treatment)
    *____ Health described (sickness; injuries; abnormalities; name of medication, if used; pretest diet)

4. Dosing method described
    ____ Amount of test material (per acre, per colony, etc.
    ____ Method of administration
    ____ Rationale for selection of method, route, or frequency

5. Test design followed (Note: Actual criteria would be determined through pre-test consultation with the Agency.)

    ____ Number of treatment levels
    ____ Number of bees per treatment level
    *____ Method of assigning bees to treatment and control groups
    *____ Method used to determine treatment levels
    ____ Size of cages or colonies, if appropriate
    ____ Number of bees per cage or colony
    ____ Number of controls
    ____ Type of controls
    ____ Environmental conditions, such as ambient temperature, humidity, weather conditions
    ____ Source and availability of food and water
    ____ Length of total observation period
    ____ Frequency and duration of each observation
    ____ Define criteria for determining effects

Criteria marked with a * are supplemental and may not be required for every study.

DISCUSSION AND RESULTS

6. ____ Observed adverse effects on bees/bee colonies due to treatments. (Graphs, printouts, and other calculations are optional).

7. ____ Detailed description of the nature, incidence, time of occurrence, severity and duration of all observed toxic effects, including death and any other abnormal or unusual signs.

8. ____ Indication of test procedures which deviated from those agreed upon during pre-test consultation with the Agency. Provide a rationale for the changes.

9. ____ Statistical methods referenced

10. The relationship between the results of the study and the test chemical described, including

    ____ Obvious problems that occurred during the study as well as the effect, if any, these problems had on the outcome of the study
    ____ Rationale for minor deviations from the protocol

Criteria marked with a * are supplemental and may not be required for every study.

141-5 Field Testing for Pollinators

GUIDANCE FOR SUMMARIZING STUDIES

Items in summary should include the items discussed in Chapter 2 of this package and the specific items listed below.

GENERAL INFORMATION

1. Conclusions summarized, including date of test initiation and termination.

MATERIALS/METHODS

2. Description of the test insects, including
   - Common and scientific names

3. Description of the dosing method, including
   - Amount of test material (per acre, per colony, etc.)
   - Method of administrations

4. Description of the test design, including
   - Number of treatment levels
   - Number of bees per treatment level
   - Size of cages or colonies, if appropriate
   - Number of bees per cage or colony
   - Number of controls
   - Type of controls
   - Define criteria for determining effects

DISCUSSION AND RESULTS

5. Observed adverse effects on bees/bee colonies due to treatments. Optional graphs, printouts, and other calculation may be attached to summary. Raw mortality data provided.

6. Detailed description of the nature, incidence, time of occurrence, severity, and duration of all observed toxic effects, including death and any other abnormal or unusual signs.

SUBDIVISION M

MICROBIALS

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151A-10 Product Identity

ACCEPTANCE CRITERIA

Does your study meet the following acceptance criteria?

1. ____ Product name and trade name (if different)
2. ____ Name, nominal concentration (for microbial ingredients, the amount present in the product in recognized units of potency, percentage of weight, units of microbial pesticide per unit weight or volume of product, or other appropriate expression of biological activity, PFU, CFU, etc.), and certified limits (upper and lower) for each active ingredient and each intentionally-added inert ingredient
3. ____ Name and upper certified limit for each impurity or each group of impurities present at $\geq$ 0.1% by weight and for certain toxicologically significant impurities (e.g., microbial toxins) present at $<$ 0.1%
4. ____ Identity and purpose of each active ingredient and each intentionally-added inert
5. ____ Taxonomic description of all living microorganisms in the product, methodologies and results of all tests performed in support of that classification, and (optional) any company assigned experimental or internal code numbers for each active microbial ingredient.
    ____ The common, alternative, and superseded names
    ____ The natural occurrence of the organism, its relationship to other species (particularly those that are pathogenic), and its history
    ____ The biological properties of the active agent with respect to target species, pest host range, life cycle, and mode of action. With respect to the properties of the microbial agent, any known or potential hazard (such as infectivity) to mammals (including humans), the environment, and nontarget species should be discussed.
    ____ A description of the morphological types of the microbial pesticide and any unusual morphological, biochemical, or resistance characteristic(s) of the organism if such characteristic(s) are different from the classic description of the organism.
    ____ If the microbial pesticide contains plasmids or other extrachromosomal genetic elements involved in pesticidal activity, pathogenicity, toxicity, etc., these must be identified as well as any known phenotypic characters coded by such elements and their stability.
6. ____ Chemical name from Chemical Abstracts Index of Nomenclature and Chemical Abstracts Service (CAS), Registry Number for each chemical active ingredient and, if available, for each intentionally-added inert
7. ____ Molecular, structural, and empirical formulas, molecular weight or weight range, and any company assigned experimental or internal code numbers for each active chemical ingredient
8. ____ Description of each beginning material in the manufacturing process for chemical ingredients
    ____ EPA Registration Number if registered; for other beginning materials, the following:
    ____ Name and address of manufacturer or supplier
    ____ Brand name, trade name or commercial designation
    ____ Technical specifications or data sheets by which manufacturer or supplier describes composition, properties or toxicity

Criteria marked with a * are supplemental and may not be required for every study.

9. ____ Culture collection from which the microbial active ingredient may be obtained.
10. ____ Similarity of currently-utilized strains to those originally registered or used as test strains for hazard testing, i.e. are they identical and, if not, provide strain designations and any known differences.
11. ____ An updated Confidential Statement of Formula (EPA Form 8570-4, rev. 9/87)

Criteria marked with a * are supplemental and may not be required for every study.

151A-11 Manufacturing Process

ACCEPTANCE CRITERIA

Does your study meet the following acceptance criteria?

1. ____ Description of manufacturing/fermentation process
2. ____ Statement of whether batch or continuous process
3. ____ Relative amounts of beginning and intermediate materials, including EPA Registration numbers, if any, source and purity of materials, and order in which they are added
4. ____ Description of equipment
5. ____ Description of physical conditions (temperature, pH, pressure, humidity) controlled in each step and the parameters that are maintained
6. ____ Description of steps taken to limit extraneous contamination both chemical and biological
7. ____ Description of the procedures used to establish the identity and purity of the culture from which the unformulated microbial pesticide is produced
8. ____ Duration of each step of process
9. ____ Description of purification procedures
10. ____ Description of the techniques used to ensure a uniform or standardized product.
11. ____ A clear presentation of the stage at which inerts are intentionally added, if and when any concentration is effected, the material to be used as the manufacturing use product (MP), whether MP registration is sought, and whether a TGAI/MP is sold and/or shipped

Criteria marked with a * are supplemental and may not be required for every study.

151A-12 Discussion of Formation of Unintended Ingredients

ACCEPTANCE CRITERIA

Does your study meet the following acceptance criteria?

1. ____ Discussion of formation of impurities based on established chemical and microbial theory addressing (1) each impurity which may be present at ≥0.1% or was found at ≥0.1% by product analyses and (2) any extraneous material that might reasonably be present in the pesticide product, e.g. allergens, microbial toxins and other metabolic products, mutant strains, microbial contaminants with particular reference to potentially infective or antagonistic forms, side products from chemical reactions employed in the manufacturing process, fermentation residues from the growth of bacteria or fungi, extraneous host residues from viruses produced in cell cultures, whole animals, or other living forms, residues of contaminants that remain following the purification or extraction process, and impurities in chemicals used in the manufacturing process.

Criteria marked with a * are supplemental and may not be required for every study.

151A-13 Analysis of Samples

ACCEPTANCE CRITERIA

Does your study meet the following acceptance criteria?

1. ____ Five or more representative samples (batches in case of batch process) analyzed for each active ingredient and all impurities or microbial contaminants present at ≥0.1%
2. ____ Degree of accountability or closure ≥ ca 98%
3. ____ Analyses conducted for certain trace toxic impurities at lower than 0.1% (examples, certain microbial toxins or nitrosamines in the case of products containing dinitroanilines or containing secondary or tertiary amines/alkanolamines plus nitrites; polyhalogenated dibenzodioxins and dibenzofurans) [Note that in the case of nitrosamines both fresh and stored samples should be analyzed.]
4. ____ Complete and detailed description of each step in analytical method used to analyze above samples. A quantitative serological or other appropriate test for the microbial pesticide may be substituted for chemical analysis.
5. ____ Statement of precision and accuracy of analytical method used to analyze above samples
6. ____ Identities and quantities (including mean and standard deviation) provided for each analyzed ingredient
7. ____ The test material is to be the purest pesticidal grade commercially produced prior to intentional addition of inerts. Generally, this test material is the same as that used for certain nontarget and human hazard testing and is identical to, or equivalent to the technical grade. Any differences from the test substance used for hazard testing should be noted.

Criteria marked with a * are supplemental and may not be required for every study.

151A-15 Certification of Limits

ACCEPTANCE CRITERIA

Does your study meet the following acceptance criteria?

1. ____ Upper and lower certified limits proposed for each active ingredient and intentionally added inert along with explanation of how the limits were determined. The limits for microbial agents should be expressed as: (i) MPCA units per unit weight or volume, (ii) international units of potency per unit weight, and (iii) weight percent of product. Items (i) and (ii) may be determined using biological, genetic, biochemical, serological, or other appropriate tests.
2. ____ Upper certified limit proposed for each impurity or microbial contaminant present at ≥ 0.1% and for certain toxicologically significant impurities at < 0.1% along with explanation of how limit determined
3. ____ Analytical methods to verify certified limits of each active ingredient and impurities (latter not required if exempt from requirement of tolerance or if generally recognized as safe by FDA) are fully described
4. ____ Analytical methods to verify certified limits validated as to their precision and accuracy

Criteria marked with a * are supplemental and may not be required for every study.

151A-16(a-j) Physical and Chemical Properties

ACCEPTANCE CRITERIA

Does your study meet the following acceptance criteria?

A. Color

____ Verbal description of coloration (or lack of it)
____ Any intentional coloration also reported in terms of Munsell color system

B. Physical State

____ Verbal description of physical state provided using terms such as "solid, granular, volatile liquid"
____ Based on visual inspection at about 20-25°C

C. Odor

____ Verbal description of odor (or lack of it) using terms such as "moldy, or "vinegar-like", etc.
____ Observed at room temperature

D. Density or Specific Gravity

____ Measured at about 20-25°C
____ Density/bulk density reported in g/ml or the specific gravity of liquids reported with reference to water at 20°C [NOTE: For a solid in particulate form a measurement of bulk density may be substituted for measurement of density, or for microbial suspensions, optical density may be used if related to colony forming units per ml]

E. pH

____ Measured at about 20-25°C
____ If material is a solid, measured after dilution or dispersion in distilled water

F. Stability

____ Sensitivity to metal ions and metal determined
____ Stability at normal and elevated temperatures
____ Sensitivity to sunlight determined
____ Determination of genetic stability as related to any toxic/pathogenic properties expressed by the MPCA

G. Storage Stability

____ Product stored in its commercial package or smaller one of same construction and materials
____ Amount of active ingredient determined in product at beginning and end of test period (duration of at least one year or for a product which degrades sufficient duration to support expiration date)

Criteria marked with a * are supplemental and may not be required for every study.

____ Any deterioration or degradation products determined
____ Product examined for physical or biological changes, or for growth and/or production of toxins at end of test
____ Product stored at about 20-25°C (and 50% relative humidity if permeable packaging) or under warehouse conditions reflecting expected storage
____ Report includes duration and conditions of storage, quantitative analyses of active ingredient, and identification of any deterioration, degradation products, or physical changes (and consequences of latter on safe handling and use of product)

H. Viscosity
____ Determined at about 20-25°C
____ Reported in poises, stokes, or other conventional units

I. Miscibility
____ Determined at about 20-25°C
____ Product mixed with petroleum solvents whose composition reflects those on label and at rate on label
____ Mixture examined for separation after 30 minutes

J. Corrosion Characteristics
____ Data on corrosion characteristics provided (experimental method described) or reasonable explanation given for lack of corrosiveness based on nature of product (e.g., lack of extreme pH; unreactive)

Criteria marked with a * are supplemental and may not be required for every study.

152A-10 Acute Oral Toxicity/Pathogenicity

ACCEPTANCE CRITERIA

Does your study meet the following acceptance criteria?

General Information

1. ____ Raw data in support of Final Report are available
2. ____ Date of test initiation and termination reported

Materials and Methods

3. Identification of test substance
   ____ Appropriate taxonomic identification of test microorganism and relationship to registered active ingredient as currently produced.

Criteria marked with a * are supplemental and may not be required for every study.

152A-11 Acute Dermal Toxicity

ACCEPTANCE CRITERIA

Does your study meet the following acceptance criteria?

1. ____ Technical form of the active ingredient tested (for reregistration only).
2.*____ At least 5 animals/sex/group
3.*____ Rats 200-300 gm, rabbits 2.0-3.0 kg, or guinea pigs 350-450 gm
4. ____ Dosing, single dermal.
5. ____ Dosing duration at least 24 hours.
6.*____ Vehicle control, only if toxicity of vehicle is unknown.
7. ____ Doses tested, sufficient to determine a toxicity category or a limit dose (2000 mg/kg).
8. ____ Application site clipped or shaved at least 24 hours before dosing
9. ____ Application site at least 10% of body surface area.
10. ____ Application site covered with a proous nonirritating cover to retain test material and to prevent ingestion.
11. ____ Individual observations (at least once a day).
12. ____ Observation period to last at least 14 days, or until all test animals appear normal, whichever is longer.
13. ____ Individual daily observations
14.*____ Individual body weights
15.*____ Gross necropsy on all animals.

Criteria marked with a * are supplemental and may not be required for every study.

152A-12 Acute Pulmonary Toxicity/Pathogenicity

ACCEPTANCE CRITERIA

Does your study meet the following acceptance criteria?

General Information

1. ____ Raw data in support of Final Report are available
2. ____ Date of test initiation and termination reported

Materials and Methods

3. Identification of test substance
    - ____ Appropriate taxonomic identification of test microorganism and relationship to registered active ingredient as currently produced.

Criteria marked with a * are supplemental and may not be required for every study.

152A-13 Acute Intravenous Toxicity/Pathogenicity

ACCEPTANCE CRITERIA

Does your study meet the following acceptance criteria?

General Information

1. ____ Raw data in support of Final Report are available
2. ____ Date of test initiation and termination reported

Materials and Methods

3. Identification of test substance
   - ____ Appropriate taxonomic identification of test microorganism and relationship to registered active ingredient as currently produced.

Criteria marked with a * are supplemental and may not be required for every study.

152A-14 Primary Eye Irritation Study

ACCEPTANCE CRITERIA

Does your study meet the following acceptance criteria?

1. ____ Technical form of the active ingredient tested (for reregistration only).
2. ____ Study not required if material is corrosive, causes severe dermal irritation or has a pH of ≤ 2 or ≥ 11.5.
3.* ____ 6 adult rabbits
4. ____ Dosing, instillation into the conjunctival sac of one eye per animal.
5.* ____ Dose, 0.1 ml if a liquid; 0.1 ml, or not more than 100mg if a solid, paste, or particulate substance.
6. ____ Solid or granular test material ground to a fine dust.
7. ____ Eyes not washed for at least 24 hours.
8. ____ Eyes examined and graded for irritation before dosing and at 1, 24, 48, and 72 hr, then daily until eyes are normal or 21 days (whichever is shorter).
9. ____ Individual daily observations.

Criteria marked with a * are supplemental and may not be required for every study.

152A-15 Hypersensitivity Incidents

ACCEPTANCE CRITERIA

Does your study meet the following acceptance criteria?

General Information

1. ____ Raw data in support of Final Report are available
2. ____ Date of test initiation and termination reported

Materials and Methods

3. Identification of test substance
   ____ Appropriate taxonomic identification of test microorganism and relationship to registered active ingredient as currently produced.

Criteria marked with a * are supplemental and may not be required for every study.

152A-16 Cell Culture

ACCEPTANCE CRITERIA

Does your study meet the following acceptance criteria?

General Information

1. ____ Raw data in support of Final Report are available
2. ____ Date of test initiation and termination reported

Materials and Methods

3. Identification of test substance
    - ____ Appropriate taxonomic identification of test microorganism and relationship to registered active ingredient as currently produced.

Criteria marked with a * are supplemental and may not be required for every study.

152A-20 Acute Toxicity

ACCEPTANCE CRITERIA

Does your study meet the following acceptance criteria?

General Information

1. ____ Raw data in support of Final Report are available
2. ____ Date of test initiation and termination reported

Materials and Methods

3. Identification of test substance
    ____ Appropriate taxonomic identification of test microorganism and relationship to registered active ingredient as currently produced.

Criteria marked with a * are supplemental and may not be required for every study.

152A-21 Subchronic Toxicity/Pathogenicity

ACCEPTANCE CRITERIA

Does your study meet the following acceptance criteria?

General Information

1. ____ Raw data in support of Final Report are available
2. ____ Date of test initiation and termination reported

Materials and Methods

3. Identification of test substance
   ____ Appropriate taxonomic identification of test microorganism and relationship to registered active ingredient as currently produced.

Criteria marked with a * are supplemental and may not be required for every study.

152A-30 Reproductive/Fertility Effects

ACCEPTANCE CRITERIA

Does your study meet the following acceptance criteria?

General Information

1. ____ Raw data in support of Final Report are available
2. ____ Date of test initiation and termination reported

Materials and Methods

3. Identification of test substance
   - ____ Appropriate taxonomic identification of test microorganism and relationship to registered active ingredient as currently produced.

Criteria marked with a * are supplemental and may not be required for every study.

152A-31 Oncogenicity

ACCEPTANCE CRITERIA

Does your study meet the following acceptance criteria?

General Information

1. ____ Raw data in support of Final Report are available
2. ____ Date of test initiation and termination reported

Materials and Methods

3. Identification of test substance
   - ____ Appropriate taxonomic identification of test microorganism and relationship to registered active ingredient as currently produced.

Criteria marked with a * are supplemental and may not be required for every study.

152A-32 Immunodeficiency

ACCEPTANCE CRITERIA

Does your study meet the following acceptance criteria?

General Information
1. ____ Raw data in support of Final Report are available
2. ____ Date of test initiation and termination reported

Materials and Methods
3. ____ Identification of test substance
   ____ Appropriate taxonomic identification of test microorganism and relationship to registered active ingredient as currently produced.

Criteria marked with a * are supplemental and may not be required for every study.

152A-33 Primate Infectivity/Pathogenicity

ACCEPTANCE CRITERIA

Does your study meet the following acceptance criteria?

General Information

1. ____ Raw data in support of Final Report are available
2. ____ Date of test initiation and termination reported

Materials and Methods

3. ____ Identification of test substance
   - ____ Appropriate taxonomic identification of test microorganism and relationship to registered active ingredient as currently produced.

Criteria marked with a * are supplemental and may not be required for every study.

153A-4 through 153A-14 Residue Chemistry

ACCEPTANCE CRITERIA

Does your study meet the following acceptance criteria?

All currently registered microbial pesticides with food uses have been granted exemptions from requirements for a tolerance. Therefore, no residue chemistry studies have been submitted in support of registration. Since techniques for conducting residue chemistry studies are specific to the unique characteristics of the microbial pesticide, it is not possible to set forth generic acceptance criteria at this time. However, all studies should include basic identification data:

1. ____ Product name and trade name (if different)
2. ____ EPA Registration Number if registered
3. ____ Taxonomic description of the active ingredient

Criteria marked with a * are supplemental and may not be required for every study.

154A-16 Acute Avian Oral Test

ACCEPTANCE CRITERIA

Does your study meet the following acceptance criteria?

1. ____ Raw data in support of final report are available
2. ____ Identity of test MPCA: genus, species and variety, strain history, identification criteria
3.*____ Type of toxins produced by strain are well defined
4. ____ Technical grade active ingredient (TGAI) used in test (see Subdivision M for TGAI definition)
5. ____ Test bird used was mallard duck or bobwhite quail
6. ____ The MPCA dose as recommended in Subdivision M
7. ____ Number of birds/treatment level(s) and controls (*10 each)
8. ____ Type of controls listed, including solvent, carrier, or whether negative or positive
9.*____ Diet and any antibiotics, vitamins or food additives described
10. ____ Observation period (*30 days)

Result reporting:

11. ____ Include LD_{50} value in mg/kg and the no-observed-effect level
12. ____ Raw mortality data provided
13. ____ Description of observed toxic effects, including death and any other abnormal signs or behavior
14. ____ Pathological changes as noted by gross necropsy examination described
15. ____ Rationale for deviations from the protocol and the effect, if any, these deviations had on the outcome of the study

Criteria marked with a * are supplemental and may not be required for every study.

154A-17 Avian Inhalation Test

ACCEPTANCE CRITERIA

Does your study meet the following acceptance criteria?

1. ____ Raw data in support of final report are available
2. ____ Identity of test MPCA: genus, species and variety, strain history, identification criteria
3.* ____ Type of toxins produced by strain are well defined
4. ____ Technical grade active ingredient (TGAI) used in test (see Subdivision M for TGAI definition)
5. ____ Test bird used was mallard duck or bobwhite quail
6. ____ The MPCA dose as recommended in Subdivision M
7. ____ Route of administration as recommended in Subdivision M
8. ____ Number of birds/treatment level(s) and controls (*10 each)
9. ____ Type of controls listed, including solvent, carrier, or whether negative or positive
10.* ____ Diet and any antibiotics, vitamins or food additives described
11. ____ Observation period (*30 days)

Result reporting:

12. ____ Include LD_{50} value in mg/kg and the no-observed-effect level
13. ____ Raw mortality data provided
14. ____ Description of observed toxic effects, including death and any other abnormal signs or behavior
15. ____ Pathological changes as noted by gross necropsy examination described
16. ____ Rationale for deviations from the protocol and the effect, if any, these deviations had on the outcome of the study

Criteria marked with a * are supplemental and may not be required for every study.

154A-18 Wild Mammal Test

ACCEPTANCE CRITERIA

Does your study meet the following acceptance criteria?

1. ____ Raw data in support of final report are available
2. ____ Identity of test MPCA: genus, species and variety, strain history, identification criteria
3.* ____ Type of toxins produced by strain are well defined
4. ____ Technical grade active ingredient (TGAI) used in test (see Subdivision M for TGAI definition)
5. ____ Test species common and scientific name provided
6. ____ The MPCA dose as recommended in Subdivision M
7. ____ Number of animals/treatment level(s) and controls (*10 each)
8. ____ Type of controls listed, including solvent, carrier, or whether negative or positive
9.* ____ Diet and any antibiotics, vitamins or food additives described
10. ____ Observation period (*30 days)

Result reporting:

11. ____ Include LD_{50} value in mg/kg and the no-observed-effect level
12. ____ Raw mortality data provided
13. ____ Description of observed toxic effects, including death, weight loss and any other abnormal signs or behavior
14. ____ Pathological changes as noted by gross necropsy examination described
15. ____ Rationale for deviations from the protocol and the effect, if any, these deviations had on the outcome of the study

Criteria marked with a * are supplemental and may not be required for every study.

154A-19 Freshwater Fish Test

ACCEPTANCE CRITERIA

Does your study meet the following acceptance criteria?

1. ____ Raw data in support of final report are available
2. ____ Identity of test MPCA: genus, species and variety, strain history, identification criteria
3.* ____ Type of toxins produced by strain are well defined
4. ____ Technical grade active ingredient (TGAI) used in test (see Subdivision M for TGAI definition)
5. ____ Test fish used was rainbow trout
6. ____ The MPCA dose as recommended in Subdivision M
7. ____ Number of fish/treatment level(s) and controls (*10 each)
8. ____ Number of treatment groups used (*5)
9. ____ Type of controls listed, including solvent, carrier, or whether negative or positive
10.* ____ Diet and any antibiotics, vitamins or food additives described
11. ____ Observation period (*minimum 30 days)

Result reporting:

12. ____ LC_{50} and/or EC_{50} value and the no-observed-effect level reported in ppm
13. ____ Raw mortality data provided
14. ____ Description of observed toxic effects, including death and any other abnormal signs or behavior
15.* ____ Pathological changes as noted by gross necropsy examination described
16. ____ Rationale for deviations from the protocol and the effect, if any, these deviations had on the outcome of the study

Criteria marked with a * are supplemental and may not be required for every study.

154A-20 Freshwater Aquatic Invertebrate Test

ACCEPTANCE CRITERIA

Does your study meet the following acceptance criteria?

1. ____ Raw data in support of final report are available
2. ____ Identity of test MPCA: genus, species and variety, strain history, identification criteria
3. ____ Type of toxins produced by strain are well defined
4. ____ Technical grade active ingredient (TGAI) used in test (see Subdivision M for TGAI definition)
5. ____ Test invertebrate used was ______ (preferrably Daphnia)
6. ____ The MPCA dose as recommended in Subdivision M
7. ____ Number of invertebtates/treatment level(s) and controls (*20 each)
8. ____ Number of treatment groups used (*5)
9. ____ Type of controls listed, including solvent, carrier, or whether negative or positive

10.* ____ Diet and any antibiotics, vitamins or food additives described

11. ____ Observation period (*30 days or until 20% mortality observed in controls; three broods for Daphnia: 14 to 21 days)

Result reporting:

12. ____ Include LC_{50} value in ppm and the no-observed-effect level
13. ____ Raw mortality data provided
14. ____ Description of observed toxic effects, including death, immobilization or other abnormal signs or behavior
15. ____ Rationale for deviations from the protocol and the effect, if any, these deviations had on the outcome of the study

Criteria marked with a * are supplemental and may not be required for every study.

154A-21 Estuarine and Marine Animal Test (Estuarine Fish)

ACCEPTANCE CRITERIA

Does your study meet the following acceptance criteria?

1. ____ Raw data in support of final report are available
2. ____ Identity of test MPCA: genus, species and variety, strain history, identification criteria
3.* ____ Type of toxins produced by strain are well defined
4. ____ Technical grade active ingredient (TGAI) used in test (see Subdivision M for TGAI definition)
5. ____ Test fish used was estuarine/marine in origin (silverside or sheepshead minnow preferred species)
6. ____ The MPCA dose as recommended in Subdivision M
7. ____ Number of fish/treatment level(s) and controls (*10 each)
8. ____ Number of treatment groups used (*5)
9. ____ Type of controls listed, including solvent, carrier, or whether negative or positive
10.* ____ Diet and any antibiotics, vitamins or food additives described
11. ____ Observation period (*minimum 30 days)

Result reporting:

12. ____ LC_{50} and/or EC_{50} value and the no-observed-effect level reported in ppm
13. ____ Raw mortality data provided
14. ____ Description of observed toxic effects, including death and any other abnormal signs or behavior
15.* ____ Pathological changes as noted by gross necropsy examination described
16. ____ Rationale for deviations from the protocol and the effect, if any, these deviations had on the outcome of the study

Criteria marked with a * are supplemental and may not be required for every study.

154A-21 Estuarine and Marine Animal Test (Estuarine Shrimp)

ACCEPTANCE CRITERIA

Does your study meet the following acceptance criteria?

1. ____ Raw data in support of final report are available
2. ____ Identity of test MPCA: genus, species and variety, strain history, identification criteria
3.* ____ Type of toxins produced by strain are well defined
4. ____ Technical grade active ingredient (TGAI) used in test (see Subdivision M for TGAI definition)
5. ____ One of the following organisms was tested: White, brown, pink, grass or mysid shrimp
6. ____ The MPCA dose as recommended in Subdivision M
7. ____ Number of shrimp/treatment level(s) and controls (*10 for static, 20 for flow-through)
8. ____ Number of treatment groups used (*5)
9. ____ Type of controls listed, including solvent, carrier, or whether negative or positive
10. ____ Diet and any antibiotics, vitamins or food additives described
11. ____ Observation period (*minimum 30 days)

Result reporting:

12. ____ LC_{50} and/or EC_{50} value and the no-observed-effect level reported in ppm
13. ____ Raw mortality data provided
14. ____ Description of observed toxic effects, including death and any other abnormal signs or behavior
15.* ____ Pathological changes as noted by gross necropsy examination described
16. ____ Rationale for deviations from the protocol and the effect, if any, these deviations had on the outcome of the study

Criteria marked with a * are supplemental and may not be required for every study.

154A-22 Nontarget Plant Studies

ACCEPTANCE CRITERIA

Does your study meet the following acceptance criteria?

1. ____ Raw data in support of final report are available
2. ____ Identity of test MPCA: genus, species and variety, strain history, identification criteria
3.*____ Type of toxins produced by strain are well defined
4. ____ Technical grade active ingredient (TGAI) used in test (see Subdivision M for TGAI definition)
5. ____ The MPCA dose was $\geq$ the maximum label application rate
6. ____ Terrestrial use test species: six species of Dicotyledoneae of at least four families and four species of Monocotyledoneae of at least two families
7. ____ For herbicidal use, test species that include plants of economic importance and those necessary for maintanace of ecosystem
8. ____ For aquatic use, test species should include Selenostrum capricornutum (freshwater green alga), Lemna gibba (duckweed), Skeletonema costatum (marine diatom), Anabaena flos-aquae (blue-green bacterium), and a freshwater diatom
9. ____ Negative and positive controls included
10. ____ Observation period

Result reporting:

11. ____ Description of observed phytotoxic/pathogenic effects and any other abnormal signs
12. ____ Rationale for deviations from protocol and the effect, if any, these deviations had on the outcome of the study

Criteria marked with a * are supplemental and may not be required for every study.

154A-23 Nontarget Insect Test

ACCEPTANCE CRITERIA

Does your study meet the following acceptance criteria?

1. ____ Raw data in support of final report are available
2. ____ Identity of test MPCA: genus, species and variety, strain history, identification criteria
3.* ____ Type of toxins produced by strain are well defined
4. ____ Technical grade active ingredient (TGAI) used in test (see Subdivision M for TGAI definition)
5. ____ The MPCA dose as recommended in Subdivision M
6. ____ Test substance incorporated in the diet
7.* ____ Diet and any antibiotics, vitamins or food additives described
8. ____ Testing was performed on three species of insect larvae representing at least two of the following groups:

*parasitic dipterans	predaceous mites
predaceous hemipterans	predaceous neuropterans
predaceous coleopterans	parasitic hymenopterans

9. ____ Number of insects/treatment level(s) and controls [(*10 each) five replicates]
10. ____ Type of controls listed, including solvent, carrier, or whether negative or positive
11. ____ Observation period 30 days or 20% mortality in normal controls

Result reporting:

12. ____ Include LD_{50} value reported in micrograms/insect larva and the no-observed-effect level
13. ____ Raw mortality data provided
14. ____ Description of observed toxic effects, including death and any other abnormal signs or behavior
15. ____ Rationale for deviations from the protocol and the effect, if any, these deviations had on the outcome of the study

Criteria marked with a * are supplemental and may not be required for every study.

154A-24 Honey Bee Test

ACCEPTANCE CRITERIA

Does your study meet the following acceptance criteria?

1. ____ Raw data in support of final report are available
2. ____ Identity of test MPCA: genus, species and variety, strain history, identification criteria
3.*____ Type of toxins produced by strain are well defined
4. ____ Technical grade active ingredient (TGAI) used in test (see Subdivision M for TGAI definition)
5. ____ The MPCA dose as recommended in Subdivision M
6. ____ Test substance incorporated in the diet
7.*____ Diet and any antibiotics, vitamins or food additives described
8. ____ Testing was conducted on the honey bee, Apis mellifera
9. ____ Number of bees/treatment level(s) and controls [(*10 each) five replicates]
10. ____ Type of controls listed, including solvent, carrier, or whether negative or positive
11. ____ Observation period 30 days or 20% mortality in normal controls

Result reporting:
12. ____ Include LD_{50} value reported in micrograms/bee and the no-observed-effect level
13. ____ Raw mortality data provided
14. ____ Description of observed toxic effects, including death and any other abnormal signs or behavior
15. ____ Rationale for deviations from the protocol and the effect, if any, these deviations had on the outcome of the study

Criteria marked with a * are supplemental and may not be required for every study.

154A-25 Terrestrial Wildlife & Aquatic Organism Testing

ACCEPTANCE CRITERIA

Does your study meet the following acceptance criteria?

TIER III

1. ____ Have submitted or are submitting with this Phase 3 Response the protocol for this study.
2. ____ Have submitted or are submitting with Phase 3 response the results of this study.

Criteria marked with a * are supplemental and may not be required for every study.

154A-26 Avian Chronic Pathogenicity and Reproduction Test

ACCEPTANCE CRITERIA

Does your study meet the following acceptance criteria?

1. ____ Raw data in support of final report are available
2. ____ Identity of test MPCA: genus, species and variety, strain history, identification criteria
3.* ____ Type of toxins produced by strain are well defined
4. ____ Technical grade active ingredient (TGAI) used in test (see Subdivision M for TGAI definition)
5. ____ Test bird used was mallard duck or bobwhite quail
6. ____ The MPCA dose as recommended in Subdivision M
7. ____ For mallards 2 males and 5 females/pen, replicated by ≥ 5 pens/treatment group, or ≥ 12 pens/treatment if individual pairs are used (For bobwhite quail one male and 2 females/pen on individual pairs)
8. ____ Number of days on which test material given
9. ____ Type of controls listed, including solvent, carrier, or whether negative or positive
10. ____ No observed effect level determined
11. ____ Days egg candled for eggshell cracks, embryo viability, and embryo survival reported

Result reporting:

12. ____ A summary of reproductive data and reproductive success data for controls and treatment levels, including 14 day hatchling survivors
13. ____ Raw mortality data provided
14. ____ Description of observed toxic effects, including death, weight loss and any other abnormal signs or behavior
15. ____ Pathological changes in abnormal birds as noted by gross necropsy examination described
16. ____ Abnormal organs add lesions cultured for presence of MPCA
17. ____ Rationale for deviations from the protocol and the effect, if any, these deviations had on the outcome of the study

Criteria marked with a * are supplemental and may not be required for every study.

154A-27 Aquatic Invertebrate Range Test

ACCEPTANCE CRITERIA

Does your study meet the following acceptance criteria?

1. ____ Have submitted or are submitting with this Phase 3 Response the protocol for this study.
2. ____ Have submitted or are submitting with Phase 3 response the results of this study.

Criteria marked with a * are supplemental and may not be required for every study.

154A-28 Fish Life Cycle Studies

ACCEPTANCE CRITERIA

Does your study meet the following acceptance criteria?

1. ____ Raw data in support of final report are available
2. ____ Identity of test MPCA: genus, species and variety, strain history, identification criteria
3.*____ Type of toxins produced by strain are well defined
4. ____ Technical grade active ingredient (TGAI) used in test (see Subdivision M for TGAI definition)
5. ____ Test fish used was one of the following species:
    silverside, sheepshead minnow, brook trout, fathead minnow, bluegill sunfish, channel catfish
6. ____ The MPCA dose as recommended in Subdivision M
7. ____ Number of fish/treatment level(s) and controls (10 each)
8. ____ Number of treatment groups used (*5)
9. ____ Type of controls listed, including solvent, carrier, or whether negative or positive
10.*____ Diet and any antibiotics, vitamins or food additives described
11. ____ Observation period one complete reproductive cycle

Result reporting:

12. ____ Weight and condition of all surviving hatchlings
13. ____ LC_{50} and/or EC_{50} value and the no-observed-effect level reported in ppm
14. ____ Stage of life cycle in which effects occurred
15. ____ Description of observed toxic effects, including death and any other abnormal signs or behavior
16.*____ Pathological changes as noted by gross necropsy examination described
17. ____ Rationale for deviations from the protocol and the effect, if any, these deviations had on the outcome of the study

Criteria marked with a * are supplemental and may not be required for every study.

154A-29 Aquatic Ecosystem Test

ACCEPTANCE CRITERIA

Does your study meet the following acceptance criteria?

1. ____ Have submitted or are submitting with this Phase 3 Response the protocol for this study.
2. ____ Have submitted or are submitting with Phase 3 response the results of this study.

Criteria marked with a * are supplemental and may not be required for every study.

154A-31 Nontarget Plant Studies

ACCEPTANCE CRITERIA

Does your study meet the following acceptance criteria?

1. ____ Have submitted or are submitting with this Phase 3 Response the protocol for this study.
2. ____ Have submitted or am submitting with Phase 3 response the results of this study.

Criteria marked with a * are supplemental and may not be required for every study.

154A-33 Simulated and Actual Field Tests (Birds, Mammals)

ACCEPTANCE CRITERIA

Does your study meet the following acceptance criteria?

TIER IV

1. ____ Have submitted or are submitting with this Phase 3 Response the protocol for this study.
2. ____ Have submitted or are submitting with Phase 3 response the results of this study.

Criteria marked with a * are supplemental and may not be required for every study.

154A-34 Simulated and Actual Field Tests (Aquatic Organisms)

ACCEPTANCE CRITERIA

Does your study meet the following acceptance criteria?

1. ____ Have submitted or are submitting with this Phase 3 Response the protocol for this study.
2. ____ Have submitted or are submitting with Phase 3 response the results of this study.

Criteria marked with a * are supplemental and may not be required for every study.

154A-35 Simulated and Actual Field Tests (Insect Predators, Parasites)

ACCEPTANCE CRITERIA

Does your study meet the following acceptance criteria?

1. ____ Have submitted or are submitting with this Phase 3 Response the protocol for this study.
2. ____ Have submitted or are submitting with Phase 3 response the results of this study.

Criteria marked with a * are supplemental and may not be required for every study.

154A-36 Simulated and Actual Field Tests (Insect Pollinators)

ACCEPTANCE CRITERIA

Does your study meet the following acceptance criteria?

1. ____ Have submitted or are submitting with this Phase 3 Response the protocol for this study.
2. ____ Have submitted or are submitting with Phase 3 response the results of this study.

Criteria marked with a * are supplemental and may not be required for every study.

155A-10 through 155A-12 Environmental Expression

ACCEPTANCE CRITERIA

Does your study meet the following acceptance criteria?

Since no currently registered microbial pesticides have exhibited significant adverse effects in Tier I Ecological Effects Studies, no Tier II Environmental Expression Studies have been required in support of registration. Since techniques for conducting environmental expression studies are specific to the unique characteristics of the microbial pesticide, it is not possible to set forth generic acceptance criteria at this time. However, all studies should include basic identification data:

1. ____ Product name and trade name (if different)
2. ____ EPA Registration Number if registered
3. ____ Taxonomic description of the active ingredient
4. ____ Description of analytical method for isolation, enumeration, and identification of the microbial pesticide, including a full analysis of the limits of detection of the analytical method.

Criteria marked with a * are supplemental and may not be required for every study.

151B-10 Product Identity

ACCEPTANCE CRITERIA

Does your study meet the following acceptance criteria?

1. ____ Product name and trade name (if different)
2. ____ Name, nominal concentration, and certified limits (upper and lower) for each active ingredient and each intentionally-added inert ingredient
3. ____ Name and upper certified limit for each impurity or each group of impurities present at $\geq$0.1% by weight and for certain toxicologically significant impurities (e.g., microbial toxins, dioxins, nitrosamines) present at <0.1%
4. ____ Purpose of each active ingredient and each intentionally-added inert
5. ____ Chemical name from Chemical Abstracts Index of Nomenclature and Chemical Abstracts Service (CAS) Registry Number for each active ingredient and, if available, for each intentionally-added inert
6. ____ Product name, trade name, and common name (if established) for each active ingredient
7. ____ Molecular, structural, and empirical formulas, molecular weight or weight range, and any company assigned experimental or internal code numbers for each active ingredient
8. ____ Description of each beginning material in the manufacturing process
    - ____ EPA Registration Number if registered; for other beginning materials, the following:
    - ____ Name and address of manufacturer or supplier
    - ____ Brand name, trade name or commercial designation
    - ____ Technical specifications or data sheets by which manufacturer or supplier describes composition, properties or toxicity
9. ____ Genus and species (and strain, subspecies, isolate, etc., if applicable) from which the biochemical was isolated or with which it is commonly associated
10. ____ Specificity of biochemical activity, the mode of action, and field rates at which the biochemical is active/proposed (units ai/A, etc.)
11. ____ Similarity to the naturally-occurring biochemical, if not derived from a biological entity.
12. ____ An updated Confidential Statement of Formula must be provided (EPA Form 8570-4 rev. 9/87).
13. ____ Any known or suspected hazards of the biochemical to man, the environment, or nontarget species.

Criteria marked with a * are supplemental and may not be required for every study.

151B-11 Manufacturing Process

ACCEPTANCE CRITERIA

Does your study meet the following acceptance criteria?

1. ____ Description of manufacturing process or extraction/isolation steps if obtained from a biological entity.
2. ____ Statement of whether batch or continuous process, if applicable
3. ____ Relative amount of beginning materials and order in which they are added
4. ____ Description of equipment
5. ____ Description of physical conditions (temperature, pH, pressure, humidity) controlled in each step and the parameters that are maintained
6. ____ Statement of whether process involves intended chemical reactions
7. ____ Flow chart with chemical equations for each intended chemical reaction
8. ____ Duration of each step of process
9. ____ Description of purification procedures
10. ____ Description of measures taken to assure quality of final product including identity of the biological source, if applicable
11. ____ A clear presentation of the stage at which inerts are intentionally added, if and when any concentration is effected, the material to be used as the manufacturing use product (MP), whether MP registration is sought, and whether a TGAI/MP is sold and/or shipped.

Criteria marked with a * are supplemental and may not be required for every study.

151B-12 Discussion of Formation of Unintended Ingredients

ACCEPTANCE CRITERIA

Does your study meet the following acceptance criteria?

1. ____ Discussion of formation of impurities based on established chemical theory addressing (1) each impurity which may be present at ≥ 0.1% or was found at ≥ 0.1% by product analyses and (2) certain toxicologically significant impurities present at < 0.1% by weight

Criteria marked with a * are supplemental and may not be required for every study.

151B-13 Analysis of Samples

ACCEPTANCE CRITERIA

Does your study meet the following acceptance criteria?

1. ____ Five or more representative samples (batches in case of batch process) analyzed for each active ingredient and all impurities present at ≥ 0.1%
2. ____ Degree of accountability or closure ≥ ca 98%
3. ____ Analyses conducted for certain trace toxic impurities at lower than 0.1% (examples, nitrosamines in the case of products containing dinitroanilines or containing secondary or tertiary amines/alkanolamines plus nitrites; polyhalogenated dibenzodioxins and dibenzofurans) [Note that in the case of nitrosamines both fresh and stored samples should be analyzed.]
4. ____ Complete and detailed description of each step in analytical method used to analyze above samples
5. ____ Statement of precision and accuracy of analytical method used to analyze above samples
6. ____ Identities and quantities (including mean and standard deviation) provided for each analyzed ingredient
7. ____ The test material is to be the purest pesticidal grade commercially produced prior to intentional addition of inerts. Generally, this test material is the same as that used for certain nontarget and human hazard testing and is identical to, or equivalent to the technical grade. Any differences from the test substance used for hazard testing should be noted.

Criteria marked with a * are supplemental and may not be required for every study.

151B-15 Certification of Limits

ACCEPTANCE CRITERIA

Does your study meet the following acceptance criteria?

1. ____ Upper and lower certified limits proposed for each active ingredient and intentionally added inert along with explanation of how the limits were determined
2. ____ Upper certified limit proposed for each impurity present at ≥ 0.1% and for certain toxicologically significant impurities at < 0.1% along with explanation of how each limit is determined
3. ____ Analytical methods to verify certified limits of each active ingredient and impurities (latter not required if exempt from requirement of tolerance or if generally recognized as safe by FDA) are fully described
4. ____ Analytical methods to verify certified limits validated as to their precision and accuracy

Criteria marked with a * are supplemental and may not be required for every study.

151B-17 Physical and Chemical Properties

ACCEPTANCE CRITERIA

Does your study meet the following acceptance criteria?

A. Color

____ Verbal description of coloration (or lack of it)

____ Any intentional coloration also reported in terms of Munsell color system

B. Physical State

____ Verbal description of physical state provided using terms such as "solid, granular, volatile liquid"

____ Based on visual inspection at about 20-25°C

C. Odor

____ Verbal description of odor (or lack of it) using terms such as "garlic-like, characteristic of aromatic compounds"

____ Observed at room temperature

D. Melting Point

____ Reported in °C

____ Any observed decomposition reported

E. Boing Point

____ Reported in °C

____ Pressure under which B.P. measured reported

____ Any observed decomposition reported

F. Density, Bulk Density, Specific Gravity

____ Measured at about 20-25°C

____ Density/bulk density reported in g/ml or the specific gravity of liquids reported with reference to water at 20°C [NOTE: For a solid in particulate form a measurement of bulk density may be substituted for measurement of density.]

G. Solubility

____ Determined in distilled water, n-octanol and representative polar and non-polar solvents, including those used in formulations and analytical methods for the pesticide

____ Measured at about 20-25°C

____ Reported in g/100ml (other units like ppm acceptable if sparingly soluble)

H. Vapor Pressure

____ Measured at ≈25°C (or calculated by extrapolation from measurements made at

Criteria marked with a * are supplemental and may not be required for every study.

higher temperature if pressure too low to measure at 25°C)

____ Experimental procedure described
____ Reported in mm Hg (torr) or other conventional units

I. pH

____ Measured at about 20-25°C
____ Measured following dilution or dispersion in distilled water

J. Stability

____ Sensitivity to metal ions and metal determined
____ Stability at normal and elevated temperatures
____ Sensitivity to sunlight determined

K. Flammability

____ Flash point reported in °F or °C
____ Flame extension or flame projection reported to nearest centimeter or nearest inch

L. Storage Stability

____ Product stored in its commercial package or smaller one of same construction and materials
____ Amount of active ingredient determined in product at beginning and end of test period (duration of at least one year or for a product which degrades sufficient duration to support expiration date)
____ Any deterioration or degradation products determined
____ Product examined for physical changes at end of test
____ Product stored at about 20-25°C (and 50% relative humidity if permeable packaging) or under warehouse conditions reflecting expected storage
____ Report includes duration and conditions of storage, quantitative analyses of active ingredient, and identification of any deterioration, degradation products, or physical changes (and consequences of latter on safe handling and use of product)

M. Viscosity

____ Determined at about 20-25°C
____ Reported in poises, stokes, or other conventional units

N. Miscibility

____ Determined at about 20-25°C
____ Product mixed with petroleum solvents whose composition reflects those on label and at rate on label
____ Mixture examined for separation after 30 minutes

Criteria marked with a * are supplemental and may not be required for every study.

O. Corrosion Characteristics

____ Data on corrosion characteristics provided (experimental method described) or reasonable explanation given for lack of corrosiveness based on nature of product (e.g., lack of extreme pH; unreactive)

P. Octanol/water Partition Coefficient

____ Measured at about 20-25°C
____ Experimentally determined and description of procedure pvided (preferred method-45 Fed. Register 77350)
____ Data supporting reported value provided

Criteria marked with a * are supplemental and may not be required for every study.

152B-10 Acute Oral Toxicity

ACCEPTANCE CRITERIA

Does your study meet the following acceptance criteria?

1. ____ Technical form of the active ingredient tested. (for reregistration only)
2.* ____ At least 5 young adult rats/sex/group
3. ____ Dosing, single oral dose or in fractions over 24 hours.
4.* ____ Vehicle control if other than water.
5. ____ Doses tested, sufficient to determine a toxicity catagy or a limit dose (5000 mg/kg).
6. ____ Individual observations at least once a day.
7. ____ Observation period to last at least 14 days, or until all test animals appear normal whichever is longer.
8. ____ Individual daily observations.
9.* ____ Individual body weights.
10.* ____ Gross necropsy on all animals.

Criteria marked with a * are supplemental and may not be required for every study.

152B-11 Acute Dermal Toxicity

ACCEPTANCE CRITERIA

Does your study meet the following acceptance criteria?

1. ____ Technical form of the active ingredient tested. (for reregistration only)
2.*____ At least 5 animals/sex/group
3.*____ Rats 200-300 gm, rabbits 2.0-3.0 kg or guinea pigs 350-450 gm.
4. ____ Dosing, single dermal.
5. ____ Dosing duration at least 24 hours.
6.*____ Vehicle control, only if toxicity of vehicle is unknown.
7. ____ Doses tested, sufficient to determine a toxicoty catagory or a limit dose (2000 mg/kg).
8. ____ Application site clipped or shaved at least 24 hours before dosing
9. ____ Application site at least 10% of body surface area.
10. ____ Application site covered with a porous nonirritating cover to retain test material and to prevent ingestion.
11. ____ Individual observations at least once a day.
12. ____ Observation period to last at least 14 days, or until all test animals appear normal whichever is longer.
13. ____ Individual daily observations.
14.*____ Individual body weights.
15.*____ Gross necropsy on all animals.

Criteria marked with a * are supplemental and may not be required for every study.

152B-12 Acute Inhalation Toxicity

ACCEPTANCE CRITERIA

Does your study meet the following acceptance criteria?

1.____ Technical form of the active ingredient tested. (for reregistration only)
2.____ Product is a gas, a solid which may produce a significant vapor hazard based on toxicity and expected use or contains particles of inhalable size for man (aerodynamic diameter 15 um or less).
3.*____ At least 5 young adult rats/sex/group
4.*____ Dosing, at least 4 hours by inhalation.
5.*____ Chamber air flow dynamic, at least 10 air changes/hour, at least 19% oxygen content.
6. ____ Chamber temperature, 22° C (±2°), relative humidity 40-60%.
7. ____ Monitor rate of air flow,
8. ____ Monitor actual concentrations of test material in breathing zone.
9. ____ Motor aerodynamic particle size for aerosols.
10.____ Doses tested, sufficient to determine a toxicity category or a limit dose (5 mg/L actual concentration of respirable substance).
11. ____ Individual observations at least once a day.
12. ____ Observation period to last at least 14 days, or until all test animals appear normal whichever is longer.
13. ____ Individual daily observations.
14.*____ Individual body weights.
15.*____ Gross necropsy on all animals.

Criteria marked with a * are supplemental and may not be required for every study.

152B-13 Primary Eye Irritation

ACCEPTANCE CRITERIA

Does your study meet the following acceptance criteria?

1. ____ Technical form of the active ingredient tested. (for reregistration only)
2. ____ Study not required if material is corrosive, causes severe dermal irritation or has a pH of ≤ 2 or ≥ 11.5.
3.*____ 6 adult rabbits
4. ____ Dosing, instillation into the conjunctival sac of one eye per animal.
5.*____ Dose, 0.1 ml if a liquid; 0.1 ml or not more than 100 mg if a solid, paste or particulate substance.
6. ____ Solid or granular test material ground to a fine dust.
7. ____ Eyes not washed for at least 24 hours.
8. ____ Eyes examined and graded for irritation before dosing and at 1, 24, 48 and 72 hr, then daily until eyes are normal or 21 days (whichever is shorter).
9. ____ Individual daily observations.

Criteria marked with a * are supplemental and may not be required for every study.

152B-14 Primary Dermal Irritation

ACCEPTANCE CRITERIA

Does your study meet the following acceptance criteria?

1. ____ Technical form of the active ingredient tested (for reregistration only)
2. ____ Study not required if material is corrosive or has a pH of ≤ 2 or ≥ 11.5.
3.* ____ 6 adult animals.
4. ____ Dosing, single dermal.
5. ____ Dosing duration 4 hours.
6. ____ Application site shaved or clipped at least 24 hour prior to dosing.
7. ____ Application site approximately 6 cm^2.
8. ____ Application site covered with a gauze patch held in place with nonirritating tape
9. ____ Material removed, washed with water, without trauma to application site
10. ____ Application site examined and graded for irritation at 1, 24, 48 and 72 hr, then daily until normal or 14 days (whichever is shorter).
11.* ____ Individual observations for the entire day of dosing.
12.* ____ Individual daily observations.

Criteria marked with a * are supplemental and may not be required for every study.

152B-15 Hypersensitivity

ACCEPTANCE CRITERIA

Does your study meet the following acceptance criteria?

1. ____ Technical form of the active ingredient tested. (for reregistration only)
2. ____ Study not required if material is corrosive or has a pH of ≤ 2 or ≥ 11.5.
3. ____ One of the following methods is utilized;
    ____ Freund's complete adjuvant test
    ____ Guinea pig maximization test
    ____ Split adjuvant technique
    ____ Buehler test
    ____ Open epicutaneous test
    ____ Mauer optimization test
    ____ Footpad technique in guinea pig
    ____ Other test accepted by OECD (specify)________
4. ____ Complete description of test
5.*____ Reference for test.
6. ____ Test followed essentially as described in reference document.
7.*____ Positive control included.

Criteria marked with a * are supplemental and may not be required for every study.

152B-17 Genotoxicity

ACCEPTANCE CRITERIA

Does your study meet the following acceptance criteria?

General Requirements

1. ____ Technical form of the active ingredient tested.
2. ____ Negative, solvent and/or vehicle control(s) for the test system.
3. ____ Positive control(s) for the test system.
4. ____ Fully identified test system, species, strain, source etc.
5. ____ Fully described method for maintaining test system.
6. ____ Fully described method for preparing test environment and administering test compound.
7. ____ Fully described metabolic activation system, if required.
8. ____ Determination of maximum and range of concentrations/doses used under test conditions.
9.*____ Criteria for determination of a positive effect.

Test Specific Requirements

Salmonella reverse mutation assay

1. ____ Minimum of four strains, TA98, TA100, TA1535 and TA1536 (alternatives need rationale).
2. ____ Strain specific positive controls.
3. ____ Highest concentration limited by toxicity, solubility or 5000 ug/plate.
4.*____ At least 5 different concentrations of test material at adequate intervals.
5.*____ A single positive response confirmed by testing over a narrow range of concentrations.
6.*____ At least three plates experimental point.

Criteria marked with a * are supplemental and may not be required for every study.

152B-18 Immunotoxicity

ACCEPTANCE CRITERIA

Does your study meet the following acceptance criteria?

1. ____ Technical form of the active ingredient tested.
2. ____ At least 10 yound adult rats or mice (either sex) per dose group per immunological parameter measured.
3. ____ Dosing duration daily for at least 30 days.
4. ____ Doses tested include signs of toxicity at high dose.
5.*____ Doses tested include a NOEL for immunotoxicity.
6.*____ Analysis for test material stability, homogenicity, and concentration in dosing medium.
7.*____ Positive control group with a known immunosuppressant if required to verify assay sensitivity.
8. ____ Individual daily observations.
9. ____ Individual body weights.
10. ____ Food and water consumption.
11. ____ Hematology
    ____ hematocrit
    ____ hemoglobin
    *____ platelet count
    ____ erythrocyte count
    ____ total and differential leucocyte count
12. ____ Spleen weights.
13. ____ Thymus weights.
14. ____ Clinical biochemistry
    ____ glucose
    *____ serum glutaric - pyruvic Transaminase
    *____ urea nitrogen
    ____ albumin
    ____ total serum protein
15. ____ Spleen and thymus cellularity and cell viability.
16* ____ Bone marrow cellularity
17. ____ Histopathology of all lesions.
18. ____ Antibody plaque forming cell assay or Immunoglobulin (IgG, IgM) quantificaion.
19. ____ One way mixed lymphocyte reaction assay or effect of test substance on induced alluyted type hypersensitivity reaction or cytotoxic T-hymprophoryte assay.
20. ____ Natural killer cell activity.
21. ____ Macrophage numbers and function.

Criteria marked with a * are supplemental and may not be required for every study.

152B-19 Mutagenicity

ACCEPTANCE CRITERIA

Does your study meet the following acceptance criteria?

Gene mutation in somatic cells in culture

1. ____ Highest concentration limited by toxicity (10-20% relative survival), solubility or 5000 ug/ml.
2.* ____ At least 4 different concentrations of test material to yield a concentration related toxic effect.
3. ____ Determination of the number of cell cultures used.

In vitro mammalian cytogenetics

1. ____ Highest concentration limited by toxicity (e.g. reduced mitotic activity; alteration of cell cycle; cytotoxicity), solubility or 5000 ug/ml.
2.* ____ Multiple concentrtions used to define the response.
3.* ____ At least two independent cultures for each experimental point.
5. ____ Determination of culture harvest time.

In vivo mammalian cytogenetics - bone marrow

1. ____ At least 5 male and 5 female animals per experimental group.
2. ____ Highest dose limited by toxicity or 5000 mg/kg.
3. ____ Determination of sampling times.

Aberrations; a) one treatment - 3 times in range of 6-48 hours after treatment adequately spaced with central sample at 24 hour (may be altered based on cell cycle time). b) repeated treatments - samples taken 6 and 24 hours after last treatment (may be altered based on cell cycle time).

Micronucleus; Samples taken 3 times, starting not earlier than 12 hours after the last treatment and at appropriate intervals following the first sample, but not beyond 72 hours.

4. ____ Micronucleus assay, at least 1000 polychromatic erythrocytes/animal scored. Ratio of poly to normochromatic determined by counting 200-1000 erythrocytes (1000 OECD).

Any mutagenicity test with suggestive or greater positive results/activity shall be submitted reqardless of missing essential items.

Criteria marked with a * are supplemental and may not be required for every study.

152B-20 Subchronic Feeding

ACCEPTANCE CRITERIA

Does your study meet the following acceptance criteria?

1. ____ Technical form of the active ingredient tested.
2. ____ At least 10 rodents or 4 nonrodents/sex/group (3 test groups and control group).
3. ____ Dosing duration daily for 90-days or 5 days/week for 13 weeks.
4. ____ Doses tested include signs of toxicity at high dose but no lethality in nonrodents or a limit dose if nontoxic (1000 mg/kg).
5. ____ Doses tested include a NOEL.
6.*____ Analysis for test material stability, homogeneity and concentration in dosing medium
7. ____ Individual daily observations.
8. ____ Individual body weights.
9. ____ Individual or cage food consumption.
10.*____ Opthalmoscopic examination (at least pretest and at term) control and high dose.
11. ____ Clinical pathology data of 12 & 13 at termination for rodents, and for non-rodents at the beginning, then either monthly or midway, and at termination.

12. ____ Hematology.
    ____ Erythrocyte count
    ____ Hemoglobin
    ____ Hematocrit
    ____ Leucocyte count
    *____ Differential count
    ____ Platelet count (or clotting measure)

13. ____ Clinical chemistry.
    *____ Alkaline phosphatase
    ____ Alanine aminotransferase
    ____ Aspartate aminotransferase
    *____ Creatinine kinase
    *____ Lactic dehydrogenase
    ____ Glucose
    ____ Bilirubin
    *____ Cholesterol
    *____ Creatinine
    ____ Total Protein
    ____ Albumin
    ____ Urea nitrogen
    ____ Inorganic phosphate
    ____ Calcium
    *____ Potassium
    ____ Sodium
    *____ Chloride

14.*____ Urinalysis, only when indicated by expected or observed activity. As scheduled in 11.
    ____ Blood
    ____ Protein
    ____ Ketone bodies
    ____ Appearance
    ____ Glucose
    ____ Total bilirubin
    *____ Urobilirubin
    ____ Sediment
    ____ Specific gravity (osmolality)
    *____ Volume

15. ____ Individual necropsy of all animals.

Criteria marked with a * are supplemental and may not be required for every study.

16. ____ Histopathology of the following tissues performed on all nonrodents and on rodents all control and high dose animals, all animals that died or were killed on study, all gross lesions on all animals, target organs on all animals and lungs, liver and kidneys on all other animals.

____ aorta
____ eyes
____ caecum
____ colon
____ duodenum
____ brain†
____ skin
____ heart
____ testes†
____ pituitary
____ ileum
____ trachea
____ gall bladder

____ jejunum
____ bone marrow
____ liver†
____ lung
____ lymph nodes
____ stomach
____ mammary gland
____ spleen†
____ musculature
____ epididymis
____ adrenals†
____ urinary bladder

____ peripheral nerve
____ kidneys†
____ esophagus
____ ovaries†
____ oviduct
____ pancreas
____ rectum
____ spinal cord (3x)
____ thyroid / parathyroids
____ salivary glands
____ thymus
____ accessory sex organs;uterus

† organs weighed

Criteria marked with a * are supplemental and may not be required for every study.

152B-21 Repeated Dermal Dose Toxicity (90-day)

ACCEPTANCE CRITERIA

Does your study meet the following acceptance criteria?

1. ____ Technical form of the active ingredient tested.
2. ____ At least 10 animals/sex/group (3 test groups and control group).
3. ____ Dosing duration at least 6 hour/day daily for 90 days or 5 days/week for 13 weeks.
4. ____ Application site at least 10% of body surface area.
5. ____ Doses tested include signs of toxicity at high dose, no or minimal dermal irritation, minimal lethality or a limit dose (1000mg/kg) if nontoxic.
6.*____ Doses tested include a NOEL.
7. ____ Individual daily observations.
8. ____ Individual body weights.
9. ____ Individual or cage food consumption.
10.*____ Opthalmoscopic examination (at least pretest and at term) control and high dose.
11. ____ Clinical pathology data of 12 & 13 in all animals at termination.

12. ____ Hematology.
    ____ Erythrocyte count
    ____ Hemoglobin
    ____ Hematocrit
    ____ Leucocyte count
    *____ Differential count
    ____ Platelet count (or clotting measure)

13. ____ Clinical chemistry.
    *____ Alkaline phosphatase
    ____ Alanine aminotransferase
    ____ Aspartate aminotransferase
    *____ Creatinine kinase
    *____ Lactic dehydrogenase
    ____ Glucose
    ____ Bilirubin
    *____ Cholesterol
    *____ Creatinine
    ____ Total Protein
    ____ Albumin
    ____ Urea nitrogen
    ____ Inorganic phosphate
    ____ Calcium
    *____ Potassium
    ____ Sodium
    *____ Chloride

14.*____ Urinalysis, only when indicated by expected or observed activity. As scheduled in 11.
    ____ Blood
    ____ Protein
    ____ Ketone bodies
    ____ Appearance
    ____ Glucose
    ____ Total bilirubin
    *____ Urobilirubin
    ____ Sediment
    ____ Specific gravity (osmolality)
    *____ Volume

15. ____ Individual necropsy of all animals.

Criteria marked with a * are supplemental and may not be required for every study.

16. ____ Histopathology of the following tissues performed on all nonrodents and rodents, all control and high dose animals, all animals that died or were killed on study, all gross lesions on all animals, target organs on all animals and lungs, liver and kidneys on all other animals.

____ aorta
____ eyes
____ caecum
____ colon
____ duodenum
____ brain†
____ skin
____ heart†
____ testes†
____ pituitary
____ ileum
____ trachea
____ gall bladder
____ jejunum
____ bone marrow
____ liver†
____ lung†
____ lymph nodes
____ stomach
____ mammary gland
____ spleen†
____ musculature
____ epididymis
____ adrenals†
____ urinary bladder
____ peripheral nerve
____ kidneys†
____ esophagus
____ ovaries†
____ oviduct
____ pancreas
____ rectum
____ spinal cord (3x)
____ thyroid / parathyroids
____ salivary glands
____ thymus
____ accessory sex organs;uterus

† organs weighed.

Criteria marked with a * are supplemental and may not be required for every study.

152B-22 Subchronic Inhalation Toxicity (90-day)

ACCEPTANCE CRITERIA

Does your study meet the following acceptance criteria?

1. ____ Technical form of the active ingredient tested (for reregistration only)
2. ____ Product is a gas, a solid which may produce a significant vapor hazard based on toxicity and expected use or contains particles of inhalable size for man (aerodynamic diameter 15 um or less).
3. ____ At least 10 young adult rats/sex/group
4. ____ Dosing, 6 hours per day, 5 days per week for 13 weeks.
5. ____ Food and water should be withheld during dosing.
6.*____ Chamber air flow dynamic, at least 10 air changes/hour, at least 19% oxygen content.
7. ____ Chamber temperature, 22° C (±2°), relative humidity 40-60%.
8.*____ Alternatively, oro-nasal or head only exposures may be used.
9. ____ Monitor rate of air flow.
10. ____ Monitor actual concentrations of test material in breathing zone.
11. ____ Monitor aerodynamic particle size for aerosols.
12. ____ Individual daily observations.
13. ____ Individual body weights.
14. ____ Individual or cage food consumption.
15.*____ Opthalmoscopic examination (at least pretest and at term) control and high dose.
16. ____ Clinical pathology data of 17 & 18 in all animals at termination.
17. ____ Hematology.
    - ____ Erythrocyte count
    - ____ Hemoglobin
    - ____ Hematocrit
    - ____ Leucocyte count
    - *____ Differential count
    - ____ Platelet count (or clotting measure)

18. ____ Clinical chemistry.
    - *____ Alkaline phosphatase
    - ____ Alanine aminotransferase
    - ____ Aspartate aminotransferase
    - *____ Creatinine kinase
    - *____ Lactic dehydrogenase
    - ____ Glucose
    - ____ Bilirubin
    - *____ Cholesterol
    - *____ Creatinine
    - ____ Total Protein
    - ____ Albumin
    - ____ Urea nitrogen
    - ____ Inorganic phosphate
    - ____ Calcium
    - *____ Potassium
    - ____ Sodium
    - *____ Chloride

Criteria marked with a * are supplemental and may not be required for every study.

19.*____ Urinalysis, only when indicated by expected or observed activity. As scheduled in 16.

____ Blood
____ Protein
____ Ketone bodies
____ Appearance
____ Glucose
____ Total bilirubin
*____ Urobilirubin
____ Sediment
____ Specific gravity (osmolality)
*____ Volume

20. ____ Individual necropsy of all animals.

21. ____ Histopathology of the following tissues performed on all nonrodents and on rodents all control and high dose animals, all animals that died or were killed on study, all gross lesions on all animals, target organs on all animals and lungs, liver and kidneys on all other animals.

____ aorta
____ eyes
____ caecum
____ colon
____ duodenum
____ brain†
____ skin
____ heart†
____ testes†
____ pituitary
____ ileum
____ trachea
____ gall bladder
____ jejunum
____ bone marrow
____ liver†
____ lung†
____ lymph nodes
____ stomach
____ mammary gland
____ spleen†
____ musculature
____ epididymis
____ adrenals†
____ urinary bladder
____ peripheral nerve
____ kidneys†
____ esophagus
____ ovaries†
____ oviduct
____ pancreas
____ rectum
____ spinal cord (3x)
____ thyroid / parathyroids
____ salivary glands
____ thymus
____ accessory sex organs;uterus

† organs weighed.

Criteria marked with a * are supplemental and may not be required for every study.

152B-23 Teratology

ACCEPTANCE CRITERIA

Does your study meet the following acceptance criteria?

1. ____ Technical form of the active ingredient tested.
2. ____ At least 20 pregnant animals/dose group for mice, rats or hamsters are available. At least 12 pregnant animals/dose group for rabbits are available (3 test groups and control group).
3. ____ At the high dose, overt maternal effects such as slight weight loss are reported as significant (or a limit dose is given, 1,000 mg/kg).
4.*____ At the low dose, no developmental toxicity is reported.
5. ____ Dosing duration is at least during the period of major organogenesis, but may extend up to one day prior to term.
6.*____ Analysis for test material stability, homogeneity and concentration in dosing medium
7. ____ Individual daily observations.
8. ____ Individual body weights.
9. ____ Individual food consumption.
10. ____ Necropsy on all animals
11. ____ Individual uterine examination including number of fetal deaths, early and late resorptions and numbers of viable fetuses per sex.
12. ____ All ovaries examined to determine number of corpora lutea.
13. ____ Individual litter weights and/or individual fetal weights per sex/litter.
14. ____ Individual fetus external examination.
15. ____ Individual fetus skeletal examination for 1/3 to 1/2 of each litter for rodents and all for all rabbits.
16. ____ Individual fetus soft tissue examination.

Criteria marked with a * are supplemental and may not be required for every study.

152B-24 Immunotoxicity – Tier II

ACCEPTANCE CRITERIA

Checklists are inappropriate at this time because consultation with the Agency is recommended prior to determining which specific tests are to be performed.

Does your study meet the following acceptance criteria?

See Special Instructions.

Criteria marked with a * are supplemental and may not be required for every study.

152B-26 Chronic Feeding

ACCEPTANCE CRITERIA

Does your study meet the following acceptance criteria?

1. ____ Technical form of the active ingredient tested.
2. ____ At least 20 rodents or 4 nonrodents/sex/group (3 test groups and control group).
3. ____ Dosing duration in rodents minimum 12 month nonfood use, 24 months food use; in nonrodents minimum 12 months[1].
4. ____ Doses tested include signs of toxicity at high dose but no lethality in nonrodents or a limit dose if nontoxic (1,000 mg/kg).
5.*____ Doses tested include a NOEL.
6.*____ Analysis for test material stability, homogeneity and concentration in dosing medium
7. ____ Individual daily observations.
8. ____ Individual body weights.
9. ____ Individual or cage food consumption.
10.*____ Opthalmoscopic examination (at least per test and at term) control and high dose.
11. ____ Clinical pathology data for all nonrodents and at least 10 rodents/group consisting of 12, 13 & 14.

12. ____ Hematology at 6 month intervals consisting of at least:
    - ____ Erythrocyte count
    - ____ Hemoglobin
    - ____ Hematocrit
    - ____ Leucocyte count
    - *____ Differential count
    - ____ Platelet count (or clotting measure)

13. ____ Clinical chemistry at 6 month intervals consisting of at least:
    - *____ Alkaline phosphatase
    - ____ Alanine aminotransferase
    - ____ Aspartate aminotransferase
    - *____ Creatinine kinase
    - *____ Lactic dehydrogenase
    - ____ Glucose
    - ____ Bilirubin
    - *____ Cholesterol
    - *____ Creatinine
    - ____ Total Protein
    - ____ Albumin
    - ____ Urea
    - ____ Inorganic phosphate
    - ____ Calcium
    - *____ Potassium
    - ____ Sodium
    - *____ Chloride

14. ____ Urinalysis at 6 month intervals consisting of at least:
    - ____ Blood
    - ____ Protein
    - ____ Ketone bodies
    - ____ Appearance
    - ____ Glucose
    - ____ Total bilirubin
    - *____ Urobilirubin
    - ____ Sediment
    - ____ Specific gravity (osmolality)
    - *____ Volume
15. ____ Individual necropsy of all animals.

Criteria marked with a * are supplemental and may not be required for every study.

16. ____ Histopathology of the following tissues performed on all nonrodents and on rodents all control and high dose animals, all animals that died or were killed on study, all gross lesions on all animals, target organs on all animals and lungs, liver and kidneys on all other animals.

____ aorta
____ eyes
____ caecum
____ colon
____ duodenum
____ brain†
____ skin
____ heart
____ testes†
____ pituitary
____ ileum
____ trachea
____ gall bladder
____ jejunum
____ bone marrow
____ liver†
____ lung
____ lymph nodes
____ stomach
____ mammary gland
____ spleen
____ musculature
____ epididymis
____ adrenals
____ urinary bladder
____ peripheral nerve
____ kidneys†
____ esophagus
____ ovaries
____ oviduct
____ pancreas
____ rectum
____ spinal cord (3x)
____ thyroid / parathyroids
____ salivary glands
____ thymus
____ accessory sex organs;uterus

† organs weighed.

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[1] Six month dog studies may be acceptable.

Criteria marked with a * are supplemental and may not be required for every study.

Subdivision M
Guideline Ref. No. 153B-29
December 24, 1989

152B-29 Oncogenicity

ACCEPTANCE CRITERIA

Does your study meet the following acceptance criteria?

1. ____ Technical form of the active ingredient tested.
2. ____ At least 50 animals/sex/group (3 test groups and control group).
3. ____ Dosing duration is at least 18 months for mice and 24 months for rats.
4. ____ Number of survivors in any group does not fall below 50% at 15 months for mice, 18 months for rats or 25% at 18 months for mice, 24 months for rats.
5. ____ Doses tested include an MTD or limit dose if nontoxic (1,000 mg/kg).
6.* ____ Doses tested include a NOEL.
7.* ____ Analysis for test material stability, homogeneity and concentration in dosing medium
8. ____ Individual daily observations.
9. ____ Individual body weights.
10. ____ Individual or cage food consumption.
11. ____ Individual necropsy of all animals.
12. ____ Blood smear from 10 animals/sex/dose at 12 and 18 months and termination. Differential count high dose and controls, all other doses if high dose shows pathology.
13. ____ Histopathology of the following tissues performed on all interim sacrifice animals, all control and high dose animals, all animals that died or were killed on study, all gross lesions on all animals, target organs on all animals and lungs, liver and kidneys on all other animals.

____ aorta
____ eyes
____ caecum
____ colon
____ duodenum
____ brain†
____ skin
____ heart
____ testes†
____ pituitary
____ ileum
____ trachea
____ gall bladder
____ jejunum
____ bone marrow
____ liver†
____ lung
____ lymph nodes
____ stomach
____ mammary gland
____ spleen†
____ musculature
____ epididymis
____ adrenals
____ urinary bladder
____ peripheral nerve
____ kidneys†
____ esophagus
____ ovaries
____ oviduct
____ pancreas
____ rectum
____ spinal cord (3x)
____ thyroid / parathyroids
____ salivary glands
____ thymus
____ accessory sex organs;uterus

† organs weighed

Criteria marked with a * are supplemental and may not be required for every study.

153B-3(a) Chemical Identity

ACCEPTANCE CRITERIA

Does your study meet the following acceptance criteria?

1. ____ Product name and trade name (if different)
2. ____ Name, nominal concentration, and certified limits (upper and lower) for each active ingredient and each intentionally-added inert ingredient
3. ____ Name and upper certified limit for each impurity or each group of impurities present at ≥ 0.1% by weight and for certain toxicologically significant impurities (e.g., dioxins, nitrosamines) present at < 0.1%
4. ____ Purpose of each active ingredient and each intentionally-added inert
5. ____ Chemical name from Chemical Abstracts Index of Nomenclature and Chemical Abstracts Service (CAS) Registry Number for each active ingredient and, if available, for each intentionally-added inert
6. ____ Product name, trade name, and common name (if established) for each active ingredient
7. ____ Molecular, structural, and empirical formulas, molecular weight or weight range, and any company assigned experimental or internal code numbers for each active ingredient
8. ____ Description of each beginning material in the manufacturing process
    - ____ EPA Registration Number if registered; for other beginning materials, the following:
    - ____ Name and address of manufacturer or supplier
    - ____ Brand name, trade name or commercial designation
    - ____ Technical specifications or data sheets by which manufacturer or supplier describes composition, properties or toxicity

Criteria marked with a * are supplemental and may not be required for every study.

153B-3(b) Directions for Use

ACCEPTANCE CRITERIA

Does your study meet the following acceptance criteria?

These criteria are intended to serve as guides for registrants to determine whether adequate directions for use are available with respect to residue chemistry considerations for each active ingredient. Registrants should check each line which has been addressed properly by product labels. A written rationale, explaining why that particular item is not pertinent, should be provided for each item that has not been addressed. Since items 6-12 on this list apply to specific types of uses, the registrant may simply write "NA" (not applicable) on the line before those types of uses which are not included on any label.

1. ____ Each formulation to be used identified with the concentration of active ingredient indicated (% by weight for solid formulations, pounds active ingredient per gallon for liquids)
2. ____ All crops which are to be treated with each formulation clearly identified
3. ____ Tolerance or exemption from tolerance proposed or established for each crop on label
4. ____ Impractical or unrealistic use restrictions not included (eg., restricting feed use of corn forage not practical due to high economic value and common practice of feeding to livestock)
5. ____ Names and quantities of stickers, spreaders, or other adjuvants to be added to spray solution
6. ____ Field and orchard crop directions
    - ____ Application rate in quantity of formulation and pounds active ingredient per acre (For row or band treatments indicate if the rate refers to the area treated or to the entire field)
    - ____ Spray volumes to be used per acre
    - ____ Maximum number applications per year or growing season
    - ____ Minimum interval between successive applications
    - ____ Minimum interval between last application and harvest (preharvest interval=PHI)
    - ____ For orchard crops additional information for full coverage sprays (quantity of formulation and pounds active ingredient per 100 gallons spray) and concentrated sprays (amount active per acre should be related to tree size)
7. ____ Aerial, ultra low volume (ULV) and mist spray directions include spray concentration, amount of active ingredient per acre, and spray volume per acre
8. ____ Postharvest fumigation directions
    - ____ Dosage expressed in weight fumigant per volume of storage space or weight fumigant per unit weight of commodity treated
    - ____ Temperature, pressure and duration of exposure specified
    - ____ Geometry and airtightness of containers described
    - ____ Aeration procedures and time of aeration specified
    - ____ Minimum interval between successive applications

Criteria marked with a * are supplemental and may not be required for every study.

9. ____ Animal treatment directions
   - ____ Concentration of pesticide in treatment solution
   - ____ Quantity of spray, pour-on solution, dust, etc. to be applied per animal
   - ____ Amount of time animal to be held in dip tank
   - ____ Frequency of treatment
   - ____ Maximum number of treatments
   - ____ Preslaughter interval (interval between last treatment and slaughter) specified (interval longer than 3 days usually not considered practical)
10. ____ Aquatic use directions
    - ____ Dosage expressed in quantity of formulation and pounds active ingredient per surface acre or parts per million pesticide in the water (in latter case the amount product per surface area should be related to average pond depth)
    - ____ Detailed description provided for specialized equipment
    - ____ Minimum distance specified from treated area to potable water or irrigation intake pipe
    - ____ If oxygen depletion problems, proportion of pond to be treated and required interval between treatments
    - ____ Maximum number of applications per year
    - ____ Minimum interval between applications
11. ____ Food handling establishment use directions
    - ____ Type of establishment that may be treated
    - ____ Dilution instructions and spray concentration
    - ____ Type of application equipment and mode of application (space spray, directed spray to crevices, spot treatment, etc.)
    - ____ Dosage limitations including cubic and square foot limitations
    - ____ Frequency of treatment
    - ____ Time of treatment (eg., after-hours in restaurants)
    - ____ Instructions concerning removal and covering of food, dishes and utensils
    - ____ Cleanup procedures before food processing, preparation or serving resumes
12. ____ Agricultural premises treatments
    - ____ Description of areas to be treated (eg., feed lot, milking room, animal barn)
    - ____ Dosage specified (pounds per unit volume treated for fogging applications; concentration of active ingredient in spray solutions; weight active ingredient per unit area of feed lot)
    - ____ Frequency of treatment
    - ____ Directions as to whether animals should be removed during treatment

Criteria marked with a * are supplemental and may not be required for every study.

153B-3(c) Nature of the Residue-Plants

ACCEPTANCE CRITERIA

Does your study meet the following acceptance criteria?

1. ___ Pesticide radiolabeled in non-labile portion of molecule (tritium label strongly discouraged)
2. ___ Specific activity sufficient to permit detection of low residue levels (0.01-0.1 ppm range)
3. ___ Radiochemically pure grade of active ingredient
4. ___ Pesticide applied to plant in manner simulating expected use
5. ___ Total radioactivity measured in plant parts used for human food or animal feed
6. ___ Extractability of residue into solvents (preferably those used in analytical enforcement method) determined
7. ___ Most of radioactivity extracted or exhaustive attempts (acid, base, enzyme) made to do so
8. ___ Major components or portion of the terminal residue identified (preferably by at least two techniques-e.g., TLC, HPLC, MS)

Criteria marked with a * are supplemental and may not be required for every study.

153B-3(d) Nature of the Residue-Animals

ACCEPTANCE CRITERIA

Does your study meet the following acceptance criteria?

1. ____ Pesticide radiolabeled in non-labile portion of molecule (tritium label strongly discouraged)
2. ____ Specific activity sufficient to permit detection of low residue levels (0.01-0.1 ppm range)
3. ____ Radiochemically pure grade of active ingredient used for dosing
4. ____ Pesticide administered orally to animals for at least three consecutive days (or applied externally according to label directions for dermal use)
5. ____ Animals not preconditioned by dosing with unlabeled material
6. ____ Animals sacrificed within 24 hours of final dose or application
7. ____ Total radioactivity measured in edible tissues (muscle, fat, liver, ruminant kidney) and milk or eggs
8. ____ Extractability of residue into solvents (preferably those used in analytical enforcement method) determined
9. ____ Most of radioactivity extracted or exhaustive attempts (acid, base, enzyme) made to do so
10. ____ Major components or portion of the terminal residue identified (preferably by at least two techniques-e.g., TLC, HPLC, MS) in edible tissues and milk or eggs

Criteria marked with a * are supplemental and may not be required for every study.

153B-3(e and f) Residue Analytical Method

ACCEPTANCE CRITERIA

Does your study meet the following acceptance criteria?

1. ____ List of equipment, reagents and standards provided along with U.S. sources/suppliers of same
2. ____ Instrumentation and operating conditions described
3. ____ Detailed description of each step in procedure to enable use by competent analyst unfamiliar with method
4. ____ Discrete response for analyte
5. ____ Control values reasonably low compared to tolerance
6. ____ Adequate recoveries (generally ≥ 70%) obtained for fortifications at the tolerance level
7. ____ Recoveries don't vary significantly from sample to sample
8. ____ Evidence that aged residues extracted by procedure (may reference work in metabolism studies)
9. ____ Data showing that method releases and recovers bound residues (if latter of toxicological concern)
10. ____ Requirements for regulatory methods (as opposed to those used only for collecting residue data)
    - ____ Does not require untreated commodity as blank
    - ____ Does not require internal or procedural standard to correct for recoveries (Addition of internal standard in final step just prior to injection is acceptable for calibration of retention times. However, use of internal standard throughout entire procedure to correct for recoveries is not acceptable unless data are available on numerous samples of each matrix to show analyte and internal standard behave identically in each step.)
    - ____ Does not require exotic equipment or reagents
    - ____ Reasonably rapid in execution
    - ____ Specific to measure residue in presence of other reasonably expected pesticides
    - ____ Sensitive in relation to tolerance
    - ____ Confirmatory method available
    - ____ Method not claimed to be Confidential Business Information
    - ____ Does not use hazardous reagents (justification needed for use of benzene as solvent or diazomethane as methylating agent)

Criteria marked with a * are supplemental and may not be required for every study.

153B-3(g) Storage Stability

ACCEPTANCE CRITERIA

Does your study meet the following acceptance criteria?

1. ____ Sample preparation and fortification described (or in cases where samples with weathered residues are used, history of crop and pesticide treatment provided)
2. ____ Storage conditions specified (temperature, containers, form of r.a.c., lighting, etc.)
3. ____ Dates of fortification (or harvest in case of field treated samples), placement into storage, sampling, and residue analysis provided
4. ____ All components of total toxic residue fortified into commodity (or present from field treatment with pesticide) and measured by validated analytical method(s) (description of latter provided or referenced)

Criteria marked with a * are supplemental and may not be required for every study.

153B-3(h) Magnitude of the Residue – Potable Water

ACCEPTANCE CRITERIA

Does your study meet the following acceptance criteria?

1. ____ Bodies of water treated according to label directions leading to maximum residues:
   - ____ Maximum application rate and number of applications
   - ____ Minimum retreatment intervals
2. ____ Data reflect modes of application on label: e.g., aerial, specialized equipment, treatment of pond margins only.
3. ____ Representative formulations examined
4. ____ Water sampled in center of treated area and at various points to show effect of distance on residue level
5. ____ Water sampled on day of treatment and later periods to show effect of time on residue level
6. ____ Sufficient number of trials conducted to determine an appropriate tolerance or maximum residue level (factors to consider include "geographic representation", seasonal and yearly variations, sizes and types of bodies of water treated, the toxicity of the pesticide)
7. ____ Total toxic residue measured in water by validated analytical method (description provided or referenced)
8. ____ Description of sample treatment, collection, handling and storage provided (covering periods from treatment to sampling and from sampling through residue analysis)
9. ____ Dates of treatment, sample collection, entry into storage, and residue analysis
10. ____ Storage stability data available reflecting storage of water samples (may be referenced to separate study)

Criteria marked with a * are supplemental and may not be required for every study.

153B-3(i) Magnitude of the Residue – Fish

ACCEPTANCE CRITERIA

Does your study meet the following acceptance criteria?

1. ____ Fish maintained in water containing maximum pesticide residues permitted by product labels
2. ____ Fish sampled on day of treatment and later periods to show effect of time on residue level and the time required for residues to plateau
3. ____ Residue data obtained for bottom feeders (e.g., catfish) and predators (e.g., bass) in the case of fish and for molluscs (e.g., clams, oysters) and crustaceans (e.g., shrimp, crabs) in the case of shellfish
4. ____ Total toxic residue measured in fish by validated analytical method (description provided or referenced)
5. ____ Analyses reflect fish commodity definitions in the Pesticide Analytical Manual, Volume I
6. ____ If pesticide used in estuarine areas, data provided for whole fish protein concentrate and smoked, canned or other processed fish products
7. ____ Description of pesticidal treatment of water and collection, handling and storage of fish samples provided
8. ____ Dates of treatment, sample collection, entry into storage, and residue analysis
9. ____ Storage stability data available reflecting storage of fish samples between sample collection (i.e., sacrifice) and residue analysis (may be referenced to separate study)

Criteria marked with a * are supplemental and may not be required for every study.

153B-3(j) Magnitude of the Residue – Irrigated Crops

ACCEPTANCE CRITERIA

Does your study meet the following acceptance criteria?

1. ____ Crops irrigated with water containing maximum pesticide residues permitted by product labels
2. ____ Representative crops from each crop grouping in 40 CFR 180.34(f) examined for residues resulting from treated irrigation water
3. ____ Crops sampled for residues within one day of irrigation
4. ____ At least two field trials conducted for each representative crop
5. ____ Total toxic residue measured in crops by validated analytical method (description provided or referenced)
6. ____ Description of pesticidal treatment of irrigation water, irrigation technique, and collection, handling and storage of crop samples provided
7. ____ Dates of pesticidal treatment of water, irrigation of crops, harvest of crops, entry of crop samples into storage, and residue analysis
8. ____ Storage stability data available reflecting storage of crop samples (may be referenced to separate study)

Criteria marked with a * are supplemental and may not be required for every study.

153B-3(k) Magnitude of the Residue – Food Handling

ACCEPTANCE CRITERIA

Does your study meet the following acceptance criteria?

1. ____ Pesticide applied in manner leading to highest residues in food that could result from actual use (factors to consider include spray concentration; type of spray [space, spot, crack and crevice]; interval between sprays if multiple applications permitted; food covered or uncovered)
2. ____ Foods representative of those to be present in treated facilities analyzed for pesticide residues (e.g., in case of cafeteria include meat, baked goods, oily food [butter, cheese], fresh fruits and vegetables)
3. ____ Foods sampled for residue analysis as soon as permitted after application and at various later times
4. ____ Pesticide residue measured in representative foods by validated analytical method (description provided or referenced)
5. ____ Description of sample treatment, collection, handling, and storage conditions/duration provided
6. ____ Storage stability data available reflecting storage of food samples from collection until residue analysis (may be referenced to separate study)

Criteria marked with a * are supplemental and may not be required for every study.

153B-3(l) Magnitude of the Residue – Meat, Milk, Poultry, Eggs

ACCEPTANCE CRITERIA

Does your study meet the following acceptance criteria?

1. ____ Compound(s) fed corresponds to residues expected on feed items
2. ____ Several dosages examined with one approximating intake expected from treated feed items, one or more representing exaggerated intake, and one control group
3. ____ Multiple animals included in each dosage group (preferably at least 3 for cattle and 10 for poultry)
4. ____ Duration of dosing adequate to ensure residues plateau in milk or eggs (preferably at least 4 weeks)
5. ____ Animals sacrificed within 24 hours of final dose
6. ____ Total toxic residue measured in edible tissues (muscle, fat, liver, cattle kidney) and milk or eggs of both control and treated animals using validated analytical method (description of latter given or referenced)
7. ____ Analytical method sufficiently sensitive (0.01-0.05 ppm)
8. ____ Description of handling and dosing of animals, feed consumption, and sample collection, handling and storage provided
9. ____ Storage stability data available reflecting storage of tissue, milk and egg samples prior to residue analysis (may be referenced to separate study)

Criteria marked with a * are supplemental and may not be required for every study.

153B-3(m) Reduction of Residues

ACCEPTANCE CRITERIA

Does your study meet the following acceptance criteria?

1. ____ Description of sample history provided for the raw agricultural commodity (r.a.c.). This could include items such as the pesticidal treatment (application rate, preharvest interval, where grown, etc.), date and location of purchase, and storage conditions from harvest or purchase until processing/washing/cooking.
2. ____ Detailed description of residue reduction procedure used on r.a.c. Such procedures may include trimming, washing, peeling, cooking, or storage of the commodity under simulated commercial or home food preparation conditions.
3. ____ Description of handling and storage of samples from time of residue reduction procedure until analysis for residues
4. ____ Total toxic residue measured with a validated analytical method (description provided or referenced) in the r.a.c. both before and after the residue reduction procedure
5. ____ Storage stability data available reflecting storage of r.a.c. and "processed" samples from time of residue reduction procedure until analysis for residues

Criteria marked with a * are supplemental and may not be required for every study.

153B-3(n) Magnitude of the Residue – Crop Field Trials

ACCEPTANCE CRITERIA

Does your study meet the following acceptance criteria?

1. ____ Crop treated according to label directions leading to maximum residues:
    ____ Maximum application rate and number of applications
    ____ Minimum retreatment intervals
    ____ Minimum preharvest interval
    ____ Minimum spray volume
2. ____ Data reflects modes of application on label: ground, aerial, oil diluents, use of adjuvants such as surfactants and spreader/stickers
3. ____ Representative formulations examined
4. ____ Trial locations represent all principal growing regions (adequate "geographic representation") OR minor crop for which regional registration is accepted
5. ____ Sufficient number of trials conducted to determine an appropriate tolerance or maximum residue level (factors to consider include seasonal and yearly variations, differences in varieties and cultural practices, the importance of the crop, the toxicity of the pesticide and its ability to translocate, and the type of use-e.g., early season/pre-emergence versus late season foliar)
6. ____ Total toxic residue measured by validated analytical method (description provided or referenced) on all parts of crop used for food or feed (except for feed items which are restricted by product labels)
7. ____ Description of sample treatment, collection, handling (including any washing or trimming) and storage provided (covering periods from planting to harvest and from harvest through analysis)
8. ____ Dates of treatment, harvest, entry into storage, and residue analysis
9. ____ Storage stability data available reflecting storage of crop samples (may be referenced to separate study)

Criteria marked with a * are supplemental and may not be required for every study.

153B-3(o) Magnitude of the Residue – Processed Food

ACCEPTANCE CRITERIA

Does your study meet the following acceptance criteria?

1. ____ The raw agricultural commodity (r.a.c.) samples that were processed contained field-treated detectable residues (preferably at or above the tolerance) OR r.a.c. was treated in the field at exaggerated rates in an attempt to get detectable residues OR spiked r.a.c.'s were used with data available to show that r.a.c. residues exist solely on the surface
2. ____ The r.a.c. was processed using procedures simulating commercial practices
3. ____ The total toxic residue was measured with a validated analytical method (description provided or referenced) in the r.a.c. and all its byproducts listed in Table 2 of the Residue Chemistry Guidelines
4. ____ Description of pesticidal treatment and processing of r.a.c. and collection, handling and storage of samples provided
5. ____ Storage stability data available reflecting storage of r.a.c. and byproduct samples (may be referenced to separate study)

Criteria marked with a * are supplemental and may not be required for every study.

154B-6 Acute Avian Oral Test

ACCEPTANCE CRITERIA

Does your study meet the following acceptance criteria?

TIER I

1. ____ Raw data in support of final report are available
2. ____ Chemical name of test substance
3. ____ Technical grade active ingredient (TGAI) used in test
4. ____ Percent active ingredient
5. ____ Name and percent of related compounds and impurities
6. ____ The pesticide dose as recommended in Subdivision M
7. ____ Test bird used was mallard duck or bobwhite quail
8. ____ Number of birds/treatment level(s) and controls (10 each)
9. ____ Type of controls listed, including solvent, carrier, or whether negative or positive
10. ____ Diet and any antibiotics, vitamins or food additives described
11. ____ Observation period (>14 days)

Result reporting:

12. ____ Include LD_{50} value in mg/kg and the no-observed-effect level
13. ____ Raw mortality data provided
14. ____ Description of observed toxic effects, including death and any other abnormal signs or behavior
15. ____ Pathological changes as noted by gross necropsy examination described

16. ____ Rationale for deviations from the protocol and the effect, if any, these deviations had on the outcome of the study

Criteria marked with a * are supplemental and may not be required for every study.

154B-7 Avian Dietary Test

ACCEPTANCE CRITERIA

Does your study meet the following acceptance criteria?

1. ____ Raw data in support of final report are available
2. ____ Chemical name of test substance
3. ____ Technical grade active ingredient (TGAI) used in test
4. ____ Percent active ingredient
5. ____ Name and percent of related compounds and impurities
6. ____ Test bird used was mallard duck or bobwhite quail
7. ____ Age at the beginning of the test is 5 to 10 days for mallard ducks and 10 to 14 days for bobwhite quail
8. ____ The pesticide dose as recommended in Subdivision M
9. ____ Number of days on test material given (5)
10. ____ Analysis of the pesticide concentration in the diet was performed
11. ____ Number of birds/treatment level(s) and controls (10 each)
12. ____ Type of controls listed, including solvent, carrier, or whether negative or positive
13. ____ Observation period (>8 days)

Result reporting:

14. ____ Include LD_{50} value in mg/kg and the no-observed-effect level
15. ____ Raw mortality data provided
16. ____ Description of observed toxic effects, including death, weight loss and any other abnormal signs or behavior
17. ____ Pathological changes in abnormal birds as noted by gross necropsy examination described
18. ____ Rationale for deviations from the protocol and the effect, if any, these deviations had on the outcome of the study

Criteria marked with a * are supplemental and may not be required for every study.

154B-8 Freshwater Fish LC_{50} Test

ACCEPTANCE CRITERIA

Does your study meet the following acceptance criteria?

1. ____ Raw data in support of final report are available
2. ____ Chemical name of test substance
3. ____ Technical grade active ingredient (TGAI) used in test
4. ____ Percent active ingredient
5. ____ Name and percent of related compounds and impurities
6. ____ Test fish used was rainbow trout
7. ____ Number of fish/treatment level(s) and controls (10 each)
8. ____ 5 treatment groups used
9. ____ The pesticide dose as recommended in Subdivision M
10. ____ Type of controls listed, including solvent, carrier, or whether negative or positive
11. ____ Observation period (minimum 96 hours)

Result reporting:

12. ____ LC_{50} and/or EC_{50} value and the no-observed-effect level reported in ppm
13. ____ Raw mortality data provided
14. ____ Description of observed toxic effects, including death and any other abnormal signs or behavior
15. ____ Pathological changes as noted by gross necropsy examination described
16. ____ Rationale for deviations from the protocol and the effect, if any, these deviations had on the outcome of the study

Criteria marked with a * are supplemental and may not be required for every study.

154B-9 Freshwater Aquatic Invertebrate LC_{50} Test

ACCEPTANCE CRITERIA

Does your study meet the following acceptance criteria?

1. ____ Raw data in support of final report are available
2. ____ Chemical name of test substance
3. ____ Technical grade active ingredient (TGAI) used in test
4. ____ Percent active ingredient
5. ____ Name and percent of related compounds and impurities
6. ____ Test invertebrate used was ________ (preferrably Daphnia)
7. ____ Pesticide dose as recommended in Subdivision M
8. ____ Number of invertebtates/treatment level(s) and controls (20 each)
9. ____ 5 treatment groups used
10. ____ Type of controls listed, including solvent, carrier, or whether negative or positive
11. ____ Diet and any antibiotics, vitamins or food additives described
12. ____ Observation period (48hr)

Result reporting:

13. ____ Include LC_{50} value in ppm and the no-observed-effect level
14. ____ Raw mortality data provided
15. ____ Description of observed toxic effects, including death, immobilization or other abnormal signs or behavior
16. ____ Rationale for deviations from the protocol and the effect, if any, these deviations had on the outcome of the study

Criteria marked with a * are supplemental and may not be required for every study.

154B-10 Nontarget Plant Studies (Seed Germination/Seedling Emergence)

ACCEPTANCE CRITERIA

Does your study meet the following acceptance criteria?

1. ____ Raw data in support of final report are available
2. ____ Chemical name of test substance
3. ____ Technical grade active ingredient (TGAI) used in test
4. ____ Percent active ingredient
5. ____ Name and percent of related compounds and impurities
6. ____ Plants tested were six dictyledoneae species from at least four families and four monocotyledoneae species from at least two families (corn, soybean, and a root crop must be included)
7. ____ Dose rates in ppm and lb ai/a at the maximum label rate
8. ____ ≥10 seeds planted/container
9. ____ ≥3 treatment groups used
10. ____ Type of controls listed, including solvent, carrier, or whether negative or positive
11. ____ Test duration and observation periods were 5 days for seed germination and two weeks for seedling emergence

Result reporting:

12. ____ Percent germination and percent emergence recorded
13. ____ Description of observed phytotoxic effects
14. ____ Rationale for deviations from the protocol and the effect, if any, these deviations had on the outcome of the study

Criteria marked with a * are supplemental and may not be required for every study.

154B-10 Nontarget Plant Studies (Vegetative Vigor)

ACCEPTANCE CRITERIA

Does your study meet the following acceptance criteria?

1. ____ Raw data in support of final report are available
2. ____ Chemical name of test substance
3. ____ Technical grade active ingredient (TGAI) used in test
4. ____ Percent active ingredient
5. ____ Name and percent of related compounds and impurities
6. ____ Plants tested were six dictyledoneae species from at least four families and four monocotyledoneae species from at least two families (corn, soybean, and a root crop must be included)
7. ____ Dose rates in ppm and pounds of active ingredient per acre (lb ai/a) at the maximum label rate
8. ____ ≥10 seeds planted/container
9. ____ ≥3 treatment groups used
10. ____ Type of controls listed, including solvent, carrier, or whether negative or positive
11. ____ Test duration and observation periods were ≥ 2 weeks

Result reporting:

12. ____ Growth measurements recorded (height and dry weight)
13. ____ Description of observed phytotoxic effects
14. ____ Percent effect as compared to control
15. ____ Rationale for deviations from the protocol and the effect, if any, these deviations had on the outcome of the study

Criteria marked with a * are supplemental and may not be required for every study.

154B-11 Nontarget Insect Testing

ACCEPTANCE CRITERIA

Does your study meet the following acceptance criteria?

1. ____ Raw data in support of final report are available
2. ____ Chemical name of test substance
3. ____ Technical grade active ingredient (TGAI) used in test
4. ____ Percent active ingredient
5. ____ Name and percent of related compounds and impurities
6. ____ The pesticide dose as recommended in Subdivision M
7. ____ Contract toxicity study, or:
8. ____ Test substance incorporated in the diet
9. ____ Diet and any antibiotics, vitamins or food additives described
10. ____ Testing was performed on three species of insect/larvae representing at least two of the following groups:
    parasitic dipterans, predaceous hemipterans, predaceous coleopterans, predaceous mites, predaceous neuropterans, parasitic hymenopterans
11. ____ Number of insects/treatment level(s) and controls (10 each) five replicates
12. ____ Type of controls listed, including solvent, carrier, or whether negative or positive
13. ____ Observation period ≥ 48 hr

Result reporting:

14. ____ Include LD_{50} value reported in micrograms/insect larva and the no-observed-effect level
15. ____ Raw mortality data provided
16. ____ Description of observed toxic effects, including death and any other abnormal signs or behavior
17. ____ Rationale for deviations from the protocol and the effect, if any, these deviations had on the outcome of the study

Criteria marked with a * are supplemental and may not be required for every study.

154B-12 Terrestrial Wildlife Testing

ACCEPTANCE CRITERIA

Does your study meet the following acceptance criteria?

TIER III

1. ____ Have submitted or are submitting with this Phase 3 Response the protocol for this study.
2. ____ Have submitted or are submitting with Phase 3 response the results of this study.

Criteria marked with a * are supplemental and may not be required for every study.

154B-13 Aquatic Animal Testing

ACCEPTANCE CRITERIA

Does your study meet the following acceptance criteria?

1. ____ Have submitted or are submitting with this Phase 3 Response the protocol for this study.
2. ____ Have submitted or are submitting with Phase 3 response the results of this study.

Criteria marked with a * are supplemental and may not be required for every study.

154B-14 Nontarget Plant Studies

ACCEPTANCE CRITERIA

Does your study meet the following acceptance criteria?

1. ____ Have submitted or are submitting with this Phase 3 Response the protocol for this study.
2. ____ Have submitted or are submitting with Phase 3 response the results of this study.

Criteria marked with a * are supplemental and may not be required for every study.

154B-15 Nontarget Insect Testing

ACCEPTANCE CRITERIA

Does your study meet the following acceptance criteria?

1. ____ Have submitted or are submitting with this Phase 3 Response the protocol for this study.
2. ____ Have submitted or are submitting with Phase 3 response the results of this study.

Criteria marked with a * are supplemental and may not be required for every study.

155B-4 Volatility Study (Lab)

ACCEPTANCE CRITERIA

Does your study meet the following acceptance criteria?

1.* ____ A greenhouse or field volatility study was provided as a substitute for this data requirement.
2. ____ A typical End Use Product (EP) was used, or an adequate explanation provided to justify the alternative chosen.
3. ____ Radiopurity and specific activity of Active Ingredient (AI)(if radiolabelled).
4. ____ The positions of the AI radiolabeling were appropriate (if radiolabelled).
5. ____ Experiments were conducted with each respectively labelled ring (for compounds containing more than one ring structure).
6. ____ Soils were completely characterized, using the USDA classification system.
7. ____ Foreign soils (if any) were adequately compared with domestic (USA) soils.
8. ____ Test substance was added to the soil at the highest recommended label rate for a single application.
9. ____ Sampling intervals were adequate.
10. ____ The decline of the AI was clearly established.
11. ____ Material balance was reasonable (>90% - <110%)
12. ____ Trapping efficiencies were reasonable.
13. ____ Reported experimental temperature was held constant (±1°C) between 18 and 30°C.
14.* ____ Volatility was reported in the correct units (ug/cm^2/hr).
15. ____ The concentration of the AI in air was measured.
16.* ____ The concentration of AI in air was reported in the correct units (ng/m^3 or ug/m^3).
17.* ____ The vapor pressure was reported in the correct units (Torr, or mm Hg), including the temperature at which it was determined.
18. ____ Appropriate analytical methods were provided.
19.* ____ Detection limits were reported.
20. ____ Raw data in support of the Final Report are available.

Criteria marked with a * are supplemental and may not be required for every study.

155B-4 Volatility Study (Field)

ACCEPTANCE CRITERIA

Does your study meet the following acceptance criteria?

1. ____ The study was conducted domestically (USA).
2. ____ A typical End Use Product (EP) was used, or an adequate explanation provided to justify the alternative chosen.
3. ____ Test substance was added to the soil at the highest recommended label rate for a single application.
4. ____ The test site (including soil type) was typical of actual use; soil was adequately characterized using the USDA classification system.
5. ____ The site used for this study was clearly shown to have no previous use history involving this (or closely related) compound (AI).
6. ____ Environmental conditions were typical, and adequately described.
7. ____ Sampling intervals were adequate.
8. ____ The decline of the AI was clearly established.
9.*____ Volatility was reported in the correct units (ug/cm^2/hr).
10. ____ The concentration of the AI in air was measured.
11.*____ The concentration of AI in air was reported in the correct units (ng/m^3 or ug/m^3).
12.*____ The vapor pressure was reported in the correct units (Torr, or mm Hg), including the temperature at which it was determined.
13. ____ Appropriate analytical methods were provided.
14.*____ Detection limits were reported.
15. ____ A storage stability study was conducted using either spiked field or spiked laboratory samples to determine the stability of samples under typical lab storage conditions.

Criteria marked with a * are supplemental and may not be required for every study.

155B-5 & 155B-6 Leaching/Adsorption/Desorption

ACCEPTANCE CRITERIA

Does your study meet the following acceptance criteria?

1. ____ Testing method was Batch Equilibrium or Soil Column.
2. ____ Analyte was the Technical Grade (TGAI) or a Pure Active Ingredient Radiolabelled (PAIRA).
3. ____ Radiopurity and specific activity of Active Ingredient (AI) (if radiolabelled).
4. ____ The positions of the AI radiolabeling were appropriate (if radiolabelled).
5. ____ Experiments were conducted with each respectively labelled ring (for compounds containing more than one ring structure.
6. ____ At least 4 soils were used, which had pH's between 4 and 8.
7. ____ One soil had a %OM < 1%.
8. ____ One of the soils was the same type of soil used in the aerobic metabolism study.
9. ____ Soils were completely characterized using the USDA classification system.
10. ____ Soils were not sieved using a screen smaller than 2mm.
11.*____ Soil moisture was maintained at 75% of 1/3 bar during the aging process.
12. ____ Foreign soils (if any) were adequately compared with domestic (USA) soils.
13. ____ Test substance was added to the soil at the highest recommended label rate for a single application.
14.*____ Material balance was reasonable (>90% - <110%).
15. ____ Mobility of parent and all major degradates identified in the laboratory metabolism studies were determined during each column leaching study.
16. ____ Raw data in support of the Final Report are available.

For SOIL TLC... (no longer recommended)

1. ____ Reference standards for degradates identified in the laboratory metabolism studies were used.
2. ____ R_f values were reported for parent and degradates.

For SOIL COLUMN...

1. ____ Elution volume was equivalent to 20" (50.8 cm times the cross-sectional area of the column).
2. ____ Column length was adequate.
3. ____ Distribution (identity and quantity) of major degradates/metabolites within the column (including eluate) was determined.

For AGED LEACHING...

1. ____ Test substance was aged for 30 days or one half-life (whichever is shorter).
2. ____ A reasonable attempt made to identify the parent and degradates.

Criteria marked with a * are supplemental and may not be required for every study.

For BATCH EQUILIBRIUM...

1. ____ Test substance was equilibrated at a minimum of 4 concentrations, with adequate time allowed for complete equilibration.
2. ____ 0.01N Ca^{++} solution was used.
3. ____ Appropriate analytical methods were provided.
4. ____ Detection limits were reported.
5. ____ K_{ads}, K_{des} and K_{oc} were reported.

Criteria marked with a * are supplemental and may not be required for every study.

155B-8 Ultraviolet Absorption Study

ACCEPTANCE CRITERIA

Does your study meet the following acceptance criteria?

1. ____ Analyte was the Technical Grade (TGAI) or a Pure Active Ingredient Radiolabelled (PAIRA).
2. ____ Radiopurity and specific activity of Active Ingredient (AI) (if radiolabelled).
3. ____ The positions of the AI radiolabeling were appropriate (if radiolabelled).
4. ____ Experiments were conducted with each respectively labeled ring (for compounds containing more than one ring structure and if radiolabeled).
5. ____ Application rate was consistent with the sensitivity of the analytical method, so that degradates could be identified.
6. ____ If natural sunlight used, record specifics regarding time of year, meteorological conditions during exposure, etc.
7. ____ If artifiacial light source used, compare light source to natural light including nature, intensity, spectrum and length of exposure
8. ____ Wavelengths <290 nm were filtered out (artificial light source).
9. ____ Dark controls maintained at same temperature as experimental chamber.
10. ____ Volatiles (if any) were trapped.
11. ____ Sampling intervals were adequate.
12. ____ Material balance was reasonable (>90% - <110%)
13. ____ A reasonable attempt was made to identify all photoproducts which exceeded 10% (yield) of the initial concentration of the AI.
14. ____ Appropriate analytical methods were provided.

15.* ____ Detection limits were reported.

16. ____ Half-lives were calculated.

Criteria marked with a * are supplemental and may not be required for every study.

155B-9 Hydrolysis Study

ACCEPTANCE CRITERIA

Does your study meet the following acceptance criteria?

1. ____ Analyte was the Technical Grade (TGAI) or a Pure Active Ingredient Radiolabelled (PAIRA).
2. ____ Radiopurity and specific activity of Active Ingredient (AI) (if radiolabelled).
3. ____ The positions of the AI radiolabeling were appropriate (if radiolabelled).
4. ____ Solubility of the AI at each pH tested.
5. ____ Concentration of AI (in solution) within the known solubility range of the AI and below 250 ppm
6. ____ Study was conducted in darkness.
7. ____ Temperature held at 25±1°C.
8. ____ Sterility of glassware, reagents, chemicals, etc. was assured.
9. ____ Volatiles (if any) were trapped.
10. ____ Solutions were buffered.
11. ____ Cosolvent (if any) did not exceed 1%.
12. ____ pH of each test solution was reported and was correct (nominally 5,7 and 9) and constant.
13. ____ Sampling intervals were adequate.
14.*____ Study was conducted for one half-life or 30 days.
15. ____ A reasonable attempt was made to identify all degradates/hydrolysates which exceeded 10% (yield) of the initial concentration of the AI.
16. ____ Material balance was reasonable (>90% -<110%).
17. ____ Appropriate analytical methods provided.
18.*____ Detection limits were reported.
19. ____ Half-lives were calculated.

Criteria marked with a * are supplemental and may not be required for every study.

155B-10 Aerobic Soil Metabolism Study

ACCEPTANCE CRITERIA

Does your study meet the following acceptance criteria?

1. ____ Analyte was the Technical Grade (TGAI) or a Pure Active Ingredient Radiolabelled (PAIRA).
2. ____ Radiopurity and specific activity of Active Ingredient (AI) (if radiolabelled).
3. ____ The positions of the AI radiolabeling were appropriate (if radiolabelled).
4. ____ Experiments were conducted with each respectively labeled ring (for compounds containing more than one ring structure and if radiolabeled).
5. ____ Soil moisture was maintained at 75% of 1/3 bar during the aging process.
6. ____ Foreign soils (if any) were adequately compared with domestic (USA) soils.
7. ____ Soil was a sandy loam, silt loam, or representative of intended use area.
8. ____ Soils were completely characterized, using the USDA classification system.
9. ____ Soils were not sieved using a screen smaller than 2mm.
10. ____ Reported experimental temperature was held between 18 and 30°C (±1°C.
11. ____ Study was conducted in darkness.
12. ____ Sampling intervals were adequate.
13. ____ Material balance was reasonable (>90% - <110%)
14. ____ Application rate was consistent with the sensitivity of the analytical method, so that degradates could be identified.
15. ____ Study was conducted until patterns of decline of parent and patterns of formation/decline of degradates were established or for no more than one year.
16.*____ Detection limits were reported.
17. ____ A reasonable attempt was made -- perhaps with multiple solvent systems -- to extract metabolites/degradates).
18. ____ A reasonable attempt was made to identify the parent and all degradates [which exceeded 10% (yield) of the initial concentration of the AI or 0.01 ppm (whichever is smaller)].
19. ____ Half-life of parent was calculated.
20. ____ Appropriate analytical methods were provided.

Criteria marked with a * are supplemental and may not be required for every study.

155B-11 Aerobic Aquatic Metabolism Study

ACCEPTANCE CRITERIA

Does your study meet the following acceptance criteria?

1. ____ Analyte was the Technical Grade (TGAI) or a Pure Active Ingredient Radiolabelled (PAIRA).
2. ____ Radiopurity and specific activity of Active Ingredient (AI)(if radiolabelled).
3. ____ The positions of the AI radiolabeling were appropriate (if radiolabelled).
4. ____ Experiments were conducted with each respectively labelled ring (for compounds containing more than one ring structure).
5.* ____ Water was adequately characterized.
6. ____ Foreign soils/sediment (if any) were adequately compared with domestic (USA) soils/sediments.
7. ____ Sediment was representative of the intended use site.
8. ____ Both aerobic and aquatic conditions were assured and maintained.
9. ____ Application rate was consistent with the sensitivityof the analytical method, so that degradates could be identified.
10. ____ Reported experimental temperature was held constant (±1°C) between 18 and 30°C).
11. ____ Sampling intervals were adequate over the 30 days of the study.
12. ____ A reasonable attempt was made to identify the parent and all degradates [which exceeded 10% of application or 0.01 ppm (whichever is smaller).
13. ____ A reasonable attempt was made -- perhaps with multiple solvent systems -- to extract metabolites/degradates.
14. ____ Half-life of parent was calculated.
15. ____ Patterns of formation and decline of major degradates were reported.
16. ____ Material balance was reasonable (>90% - <110%)
17.* ____ Detection limits were reported.
18. ____ Appropriate analytical methods were provided.

Criteria marked with a * are supplemental and may not be required for every study.

155B-12 Photolysis in Soil Study

ACCEPTANCE CRITERIA

Does your study meet the following acceptance criteria?

1. ____ Analyte was the Technical Grade (TGAI) or a Pure ActiveIngredient Radiolabelled (PAIRA).
2. ____ Radiopurity and specific activity of Active Ingredient (AI) (if radiolabelled).
3. ____ The positions of the AI radiolabeling were appropriate (if radiolabelled).
4. ____ Experiments were conducted with each respectively labeled ring (for compounds containing more than one ring structure and if radiolabeled).
5. ____ Soils were completely characterized, using the USDA classification system.
6. ____ Soils were not sieved using a screen smaller than 2 mm.
7.*____ Soil moisture was maintained at 75% of 1/3 bar during the aging process.
8. ____ Foreign soils (if any) were adequately compared with domestic (USA) soils.
9. ____ At least one of the soils was the same type as was used in the aerobic metabolism study.
10. ____ Soil was vital (not sterilized).
11. ____ Application rate was consistent with the sensitivity of the analytical method, so that degradates could be identified.
12. ____ Volatiles (if any) were trapped.
13. ____ If natural sunlight used, redord specifics regarding time of year, meteorological conditions during exposure, etc.
14. ____ If artificial light source used, compare light source to natural light including nature, intensity, spectrum and length of exposure.
15. ____ Wavelengths <290 nm were filtered out (artificial light source).
16. ____ Dark controls maintained at same temperature as exposed soils.
17. ____ Reported experimental temperature was held between 20 and 30°C.
18. ____ Sampling intervals were adequate.
19. ____ Material balance was reasonable (>90 - <110%).
20. ____ A reasonable attempt was made at each sample time to identify all photoproducts which exceeded 10% (yield) of the initial concentration of the AI.
21. ____ Appropriate analytical methods were provided.
22.*____ Detection limits were reported.
23. ____ Half-lives were calculated and reported.

Criteria marked with a * are supplemental and may not be required for every study.

155B-13 Photolysis in Water Study

ACCEPTANCE CRITERIA

Does your study meet the following acceptance criteria?

1. ____ Analyte was the Technical Grade (TGAI) or a Pure Active Ingredient Radiolabelled (PAIRA).
2. ____ Radiopurity and specific activity of Active Ingredient (AI) (if radiolabelled).
3. ____ The positions of the AI radiolabeling were appropriate (if radiolabelled).
4. ____ Solubility of the AI.
5. ____ Concentration of the AI (in solution) within the known solubility range of the AI, and below 250 ppm.
6. ____ Volatiles (if any) were trapped.
7. ____ Solutions buffered at the pH of minimal hydrolysis, a pH between 5 and 9.
8. ____ Cosolvent (if any) did not exceed 1% and was definitely not known photosensitizer.
9. ____ If natural sunlight used, record specifics regarding time of year, meteorological conditions during exposure, etc.
10. ____ If artificial light source used, compare light source to natural light including nature, intensity, spectrum and length of exposure.
11. ____ Wavelengths <290 nm were filtered out (artificial lightsource).
12. ____ Dark controls maintained at same temperature as exposed solutions.
13. ____ Reported experimental temperature was held at 25±1°C.
14. ____ Sterility of glassware, reagents, chemicals, etc. was assured.
15. ____ Sampling intervals were adequate.
16. ____ Material balance was reasonable (>90% - <110%)
17. ____ A reasonable attempt was made at all ampling times to identify all degradates/hydrolysates which exceed 10% (yield) of the initial concentration of the AI.
18. ____ Appropriate analytical methods were provided.
19.* ____ Detection limits were reported.
20. ____ Half-lives were calculated.

Criteria marked with a * are supplemental and may not be required for every study.

SUBDIVISION N

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161-1 Hydrolysis

ACCEPTANCE CRITERIA

Does your study meet the following acceptance criteria?

1. ____ Test substance was the Technical Grade (TGAI) or a Pure Active Ingredient Radiolabeled (PAIRA).

2. ____ Radiopurity and specific activity of Active Ingredient (AI) (if radiolabeled).

3. ____ The positions of the AI radiolabeling were appropriate (if radiolabeled).

4. ____ Solubility of the AI at each pH tested.

5. ____ Concentration of AI (in solution) within the known solubility range of the AI and below 250 ppm

6. ____ Study was conducted in darkness.

7. ____ Temperature held at 25±1°C.

8. ____ Sterility of glassware, reagents, chemicals, etc. was assured.

9. ____ Volatiles (if any) were trapped.

10. ____ Solutions were buffered.

11. ____ Cosolvent (if any) did not exceed 1%.

12. ____ pH of each test solution was reported and was correct (nominally 5,7 and 9) and constant.

13. ____ Sampling intervals were adequate.

14.*____ Study was conducted for one half-life or 30 days.

15. ____ A reasonable attempt was made to identify all degradates/hydrolysates which exceeded 10% (yield) of the initial concentration of the AI.

16. ____ Material balance was reasonable (>90% -<110%).

17. ____ Appropriate analytical methods provided.

18.*____ Detection limits were reported.

Criteria marked with a * are supplemental and may not be required for every study.

19. ____ Half-lives were calculated.

Criteria marked with a * are supplemental and may not be required for every study.

161-1 Hydrolysis

GUIDANCE FOR SUMMARIZING STUDIES

Items in summary should include the items discussed in Chapter 2 of this package and the specific items listed below.

A. **Summary of Conclusions**

B. **Test Material**

1. The chemical structure: (for radiolabeled substances include '*' to indicate label position)
2. The purity of the test substance (for radiolabeled substances include radiopurity and specific activity)
3. Solubility of the test material in water (include temperature and pH)
4. Reference additional studies that are presented to satisfy this data requirement, that use alternate radiolabeling and that are included in this summary package

C. **Test Methodology**

1. Level of fortification
2. Light conditions during study
3. Temperature range during experiment
4. Sterility measures during experiment (if used)
5. Description of water source and characteristics (including pH, conductivity, hardness, etc)
6. Description of pH's and buffer solutions
7. Description of cosolvent and concentration (if any)
8. Description of sampling intervals including time zero concentration: (indicate hr, day, weeks)
9. Description of volatility trap and analysis procedures (if for radiolabeled substances included)
10. Description of extraction method for parent material and individual degradates
11. Description of extraction efficiency as percent of applied individually for parent and degradates
12. Description of analytical method including standards used and percent recovery
13. Description of storage conditions

14. Description of storage stability and results

E. **Reported Results**

1. Description of material balance at sampling intervals as percent of applied
2. Description of half-life calculation for parent and degradates
3. Description or graph of formation and decline of parent and degradates

F. **Discussion of Results**

161-2 Photodegradation in Water
ACCEPTANCE CRITERIA

Does your study meet the following acceptance criteria?

1. ____ Test substance was the Technical Grade (TGAI) or a Pure Active Ingredient Radiolabeled (PAIRA).
2. ____ Radiopurity and specific activity of Active Ingredient (AI) (if radiolabeled).
3. ____ The positions of the AI radiolabeling were appropriate (if radiolabeled).
4. ____ Solubility of the AI.
5. ____ Concentration of the AI (in solution) within the known solubility range of the AI, and below 250 ppm.
6. ____ Volatiles (if any) were trapped.
7. ____ Solutions buffered at the pH of minimal hydrolysis, a pH between 5 and 9.
8. ____ Cosolvent (if any) did not exceed 1% and was definitely not known photosensitizer.
9. ____ If natural sunlight used, record specifics regarding time of year, meteorological conditions during exposure, etc.
10. ____ If artificial light source used, compare light source to natural light including nature, intensity, spectrum and length of exposure.
11. ____ Wavelengths <290 nm were filtered out (artificial light source).
12. ____ Dark controls maintained at same temperature as exposed solutions.
13. ____ Reported experimental temperature was held at 25±1°C.
14. ____ Sterility of glassware, reagents, chemicals, etc. was assured.
15. ____ Sampling intervals were adequate.
16. ____ Material balance was reasonable (>90% - <110%)
17. ____ A reasonable attempt was made at all sampling times to identify all degradates/hydrolysates which exceed 10% (yield) of the initial concentration of the AI.

Criteria marked with a * are supplemental and may not be required for every study.

18. ____ Appropriate analytical methods were provided.

19.*____ Detection limits were reported.

20. ____ Half-lives were calculated.

Criteria marked with a * are supplemental and may not be required for every study.

161-2 Photodegradation in Water

GUIDANCE FOR SUMMARIZING STUDIES

Items in summary should include the items discussed in Chapter 2 of this package and the specific items listed below.

A. **Summary of Conclusions**

B. **Test Material**

1. The chemical structure: (for radiolabeled substances include '*' to indicate label position)
2. The purity of the test substance (for radiolabeled substances include radiopurity and specific activity)
3. Solubility of the test material in water (include temperature and pH)
4. Reference additional studies that are presented to satisfy this data requirement, that use alternate radiolabeling and that are included in this summary package

C. **Test Methodology**

1. Level of fortification
2. Description of light source

    a.If natural, describe time of year, meteorological conditions, actual photoperiod and other variables affecting light intensity (include latitude and longitude)

    b.If artificial, indicate light source, intensity, spectrum, dark/light photoperiod as compared to natural sunlight and whether or not wavelengths <290 nm filtered out

3. Temperature range during experiment
4. Description of dark controls
5. Description of water source and characteristics (including pH, conductivity, hardness, etc)
6. Description of pH's and buffer solutions
7. Description of cosolvent and concentration (if any)
8. Description of sampling intervals including time zero concentration: (indicate hr, day, weeks)
9. Description of volatility trap and analysis procedures (if used)
10. Description of extraction method for parent material and individual degradates

11. Description of extraction efficiency as percent of applied individually for parent and degradates
12. Description of analytical method including standards used and percent recovery
13. Description of storage conditions
14. Description of storage stability and results

E. **Reported Results**

1. Description of material balance at sampling intervals as percent of applied
2. Description of half-life calculation for parent and degradates
3. Description or graph of formation and decline of parent and degradates

F. **Discussion of Results**

161-3 Photodegradation on Soil

ACCEPTANCE CRITERIA

Does your study meet the following acceptance criteria?

1. ____ Test substance was the Technical Grade (TGAI) or a Pure Active Ingredient Radiolabeled (PAIRA).

2. ____ Radiopurity and specific activity of Active Ingredient (AI) (if radiolabeled).

3. ____ The positions of the AI radiolabeling were appropriate (if radiolabeled).

4. ____ Experiments were conducted with each respectively labeled ring (for compounds containing more than one ring structure and if radiolabeled).

5. ____ Soils were completely characterized, using the USDA classification system.

6. ____ Soils were not sieved using a screen smaller than 2 mm.

7.* ____ Soil moisture was maintained at 75% of 1/3 bar during the aging process.

8. ____ Foreign soils (if any) were adequately compared with domestic (USA) soils.

9. ____ At least one of the soils was the same type as was used in the aerobic metabolism study.

10. ____ Soil was vital (not sterilized).

11. ____ Application rate was consistent with the sensitivity of the analytical method, so that degradates could be identified.

12. ____ Volatiles (if any) were trapped.

13. ____ If natural sunlight used, record specifics regarding time of year, meteorological conditions during exposure, etc.

14. ____ Artificial light.
    ____ If artificial light source used, compare light source to natural light including nature, intensity, spectrum and length of exposure.
    ____ If artificial light source used, light/dark photoperiod approximated natural conditions (12 hr: 12 hr, 16 hr: 8 hr, etc.).

15. ____ Wavelengths <290 nm were filtered out (artificial light source).

16. ____ Dark controls maintained at same temperature as exposed soils.

Criteria marked with a * are supplemental and may not be required for every study.

17. ____ Reported experimental temperature was held constant (±1°C) between 18 and 30°C.

18. ____ Sampling intervals were adequate.

19. ____ Material balance was reasonable (>90 - <110%).

20. ____ A reasonable attempt was made at each sample time to identify all photoproducts which exceeded 10% (yield) of the initial concentration of the AI.

21. ____ Appropriate analytical methods were provided.

22.*____ Detection limits were reported.

23. ____ Half-lives were calculated and reported.

Criteria marked with a * are supplemental and may not be required for every study.

161-3 Photodegradation on Soil

GUIDANCE FOR SUMMARIZING STUDIES

Items in summary should include the items discussed in Chapter 2 of this package and the specific items listed below.

A. **Summary of Conclusions**

B. **Test Material**

1. The chemical structure: (for radiolabeled substances include '*' to indicate label position)
2. The purity of the test substance (for radiolabeled substances include radiopurity and specific activity)
3. Solubility of the test material in water (include temperature and pH)
4. Reference additional studies that are presented to satisfy this data requirement, that use alternate radiolabeling and that are included in this summary package

C. **Soil description**

1. Description of test soil source (including country, state of origin, etc) for each soil used
2. Description test soil type (USDA classification)
3. Description of soil characteristics
    a. % sand, silt, clay
    b. % organic material
    c. pH
    d. Cation exchange capacity (meq/100 grams)
4. Comparison of foreign soil (if used), including soil characteristics (noted above) and microbial activity, to U.S. soils
5. Description of soil preparation including sieve size and sterilization technique (if used)
6. Indicate other studies supporting this registration which use this soil type

D. **Test Methodology**

1. Level of fortification

2. Description of light source

   a. If natural, describe time of year, meteorological conditions, actual photoperiod and other variables affecting light intensity (include latitude and longitude)

   b. If artificial, indicate light source, intensity, spectrum, dark/light photoperiod as compared to natural sunlight and whether or not wavelengths <290 nm filtered out

3. Temperature range during experiment

4. Description of dark controls

5. Description of sampling intervals including time zero concentration: (indicate hr, day, weeks)

6. Description of volatility trap and analysis procedures (if used)

7. Description of extraction method for parent material and individual degradates

8. Description of extraction efficiency as percent of applied individually for parent and degradates

9. Description of analytical method including standards used and percent recovery

10. Description of storage conditions

11. Description of storage stability and results

E. **Reported Results**

1. Description of material balance at sampling intervals as percent of applied

2. Description of half-life calculation for parent and degradates

3. Description or graph of formation and decline of parent and degradates

F. **Discussion of Results**

161-4 Photodegradation in Air

ACCEPTANCE CRITERIA

Does your study meet the following acceptance criteria?

1. ____ Test substance was the Technical Grade (TGAI) or a Pure Active Ingredient Radiolabeled (PAIRA).

2. ____ Radiopurity and specific activity of Active Ingredient (AI) (if radiolabeled).

3. ____ The positions of the AI radiolabeling were appropriate (if radiolabeled).

4. ____ Experiments were conducted with each respectively labeled ring (for compounds containing more than one ring structure and if radiolabeled).

5. ____ Application rate was consistent with the sensitivity of the analytical method, so that degradates could be identified.

6. ____ If natural sunlight used, record specifics regarding time of year, meteorological conditions during exposure, etc.

7. ____ If artificial light source used, compare light source to natural light including nature, intensity, spectrum and length of exposure

8. ____ Wavelengths <290 nm were filtered out (artificial light source).

9. ____ Dark controls maintained at same temperature as experimental chamber.

10. ____ Volatiles (if any) were trapped.

11. ____ Sampling intervals were adequate.

12. ____ Material balance was reasonable (>90% - <110%)

13. ____ A reasonable attempt was made to identify all photoproducts which exceeded 10% (yield) of the initial concentration of the AI.

14. ____ Appropriate analytical methods were provided which clearly distinguished between vapor-phase and solution (if any) phase photoproducts.

15.*____ Detection limits were reported.

16. ____ Half-lives were calculated.

Criteria marked with a * are supplemental and may not be required for every study.

161-4 Photodegradation in Air

GUIDANCE FOR SUMMARIZING STUDIES

Items in summary should include the items discussed in Chapter 2 of this package and the specific items listed below.

A. **Summary of Conclusions**

B. **Test Material**

1. The chemical structure: (for radiolabeled substances include '*' to indicate label position)
2. The purity of the test substance (for radiolabeled substances include radiopurity and specific activity)
3. Solubility of the test material in water (include temperature and pH)
4. Reference additional studies that are presented to satisfy this data requirement, that use alternate radiolabeling and that are included in this summary package

C. **Test Methodology**

1. Level of fortification
2. Description of light source
   a. If natural, describe time of year, meteorological conditions, actual photoperiod and other variables affecting light intensity (include latitude and longitude)
   b. If artificial, indicate light source, intensity, spectrum, dark/light photoperiod as compared to natural sunlight and whether or not wavelengths <290 nm filtered out
3. Temperature range during experiment
4. Description of dark controls
5. Description of sampling intervals including time zero concentration: (indicate hr, day, weeks)
6. Description of volatility trap and analysis procedures (if used)
7. a. Description of extraction method for parent material and individual degradates
   b. Description of method used to distinguish between vapor phase and solution phase degradates.
8. Description of extraction efficiency as percent of applied individually for parent and degradates
9. Description of analytical method including standards used and percent recovery

10. Description of storage conditions
11. Description of storage stability and results

E. **Reported Results**

1. Description of material balance at sampling interval as percent of applied
2. Description of half-life calculation for parent and degradates
3. Description or graph of formation and decline of parent and degradates

F. **Discussion of Results**

162-1 Aerobic Soil Metabolism

ACCEPTANCE CRITERIA

Does your study meet the following acceptance criteria?

1. ____ Test substance was the Technical Grade (TGAI) or a Pure Active Ingredient Radiolabeled (PAIRA).

2. ____ Radiopurity and specific activity of Active Ingredient (AI) (if radiolabeled).

3. ____ The positions of the AI radiolabeling were appropriate (if radiolabeled).

4. ____ Experiments were conducted with each respectively labeled ring (for compounds containing more than one ring structure and if radiolabeled).

5. ____ Soil moisture was maintained at 75% of 1/3 bar during the aging process.

6. ____ Foreign soils (if any) were adequately compared with domestic (USA) soils.

7. ____ Soil was a sandy loam, silt loam, or representative of intended use area.

8. ____ Soils were completely characterized, using the USDA classification system.

9. ____ Soils were not sieved using a screen smaller than 2mm.

10. ____ Reported experimental temperature was held constant (±1°C) between 18 and 30°C.

11. ____ Study was conducted in darkness.

12. ____ Sampling intervals were adequate.

13. ____ Material balance was reasonable (>90% - <110%)

14. ____ Application rate was consistent with the sensitivity of the analytical method, so that degradates could be identified.

15. ____ Study was conducted until patterns of decline of parent and patterns of formation/decline of degradates were established or for no more than one year.

16.*____ Detection limits were reported.

Criteria marked with a * are supplemental and may not be required for every study.

17. ____ A reasonable attempt was made -- perhaps with multiple solvent systems -- to extract metabolites/degradates).

18. ____ A reasonable attempt was made to identify the parent and all degradates [which exceeded 10% (yield) of the initial concentration of the AI or 0.01 ppm (whichever is smaller)].

19. ____ Half-life of parent was calculated.

20. ____ Appropriate analytical methods were provided.

Criteria marked with a * are supplemental and may not be required for every study.

162-1 Aerobic Soil Metabolism

GUIDANCE FOR SUMMARIZING STUDIES

Items in summary should include the items discussed in Chapter 2 of this package and the specific items listed below.

A. Summary of Conclusions

B. Test Material

1. The chemical structure: (for radiolabeled substances include '*' to indicate label position)

2. The purity of the test substance (for radiolabeled substances include radiopurity and specific activity)

3. Solubility of the test material in water (include temperature and pH)

4. Reference additional studies that are presented to satisfy this data requirement, that use alternate radiolabeling and that are included in this summary package

C. Soil description

1. Description of test soil source (including country, state of origin, etc) for each soil used

2. Description test soil type (USDA classification)

3. Description of soil characteristics

    a. % sand, silt, clay

    b. % organic material

    c. pH

    d. Cation exchange capacity (meq/100 grams)

4. Comparison of foreign soil (if used), including soil characteristics (noted above) and microbial activity, to U.S. soils

5. Description of soil preparation including sieve size

6. Indicate other studies supporting this registration which use this soil

D. **Test Methodology**

1. Level of fortification
2. Description of treatment technique
3. Description of soil moisture content throughout study
4. Temperature range during experiment
5. Description of method used to initiate and maintain aerobic conditions
6. Description of sampling intervals including time zero concentration: (indicate hr, day, weeks)
7. Description of volatility trap and analysis procedures (if used)
8. Description of extraction method for parent material and individual degradates
9. Description of extraction efficiency as percent of applied individually for parent and degradates
10. Description of analytical method including standards used and percent recovery
11. Description of storage conditions
12. Description of storage stability and results

E. **Reported Results**

1. Description of material balance at sampling intervals as percent of applied
2. Description of half-life calculation for parent and degradates
3. Description or graph of formation and decline of parent and degradates
4. Description of aerobicity measurement (Eh) and results if measured.

F. **Discussion of Results**

162-2 Anaerobic Soil Metabolism

ACCEPTANCE CRITERIA

Does your study meet the following acceptance criteria?

1. ____ Test substance was the Technical Grade (TGAI) or a Pure Active Ingredient Radiolabeled (PAIRA).

2. ____ Radiopurity and specific activity of Active Ingredient (AI) (if radiolabeled).

3. ____ The positions of the AI radiolabeling were appropriate (if radiolabeled).

4. ____ Experiments were conducted with each respectively labelled ring (for compound containing more than one ring structure).

5.*____ Soil moisture was maintained at 75% of 1/3 bar during the aging process.

6. ____ Foreign soils (if any) were adequately compared with domestic (USA) soils.

7. ____ Soil was a sandy loam, silt loam, or representative of intended use area.

8. ____ Soils were completely characterized, using the USDA classification system.

9. ____ Soils were not sieved using a screen smaller than 2mm.

10. ____ Reported experimental temperature was held constant (±1°C) between 18 and 30°C.

11. ____ Study was conducted in darkness.

12. ____ Sampling intervals were adequate.

13. ____ Material balance was reasonable (>90% - <110%)

14. ____ Application rate was consistent with the sensitivity of the analytical method, so that degradates could be identified.

15. ____ Treated soil was aged for one half-life or 30 days (whichever is shorter) prior to initiation of anaerobic conditions.

16. ____ Study was conducted until patterns of decline of parent and patterns of formation decline of degradates were established or for no more than 60 days.

17.*____ Detection limits were reported.

Criteria marked with a * are supplemental and may not be required for every study.

18. ____ A reasonable attempt was made to identify the parent and all degradates [which exceeded 10% of initial application or 0.01 ppm (whichever is smaller)].

19. ____ The unextractable fraction was reasonable (i.e. a reasonable attempt was made -- perhaps with multiple solvent systems -- to extract metabolites/degradates).

20. ____ Half-life of parent was provided.

21. ____ Appropriate analytical methods were provided.

Criteria marked with a * are supplemental and may not be required for every study.

162-2 Anaerobic Soil Metabolism

GUIDANCE FOR SUMMARIZING STUDIES

Items in summary should include the items discussed in Chapter 2 of this package and the specific items listed below.

A. **Summary of Conclusions**

B. **Test Material**

1. The chemical structure: (for radiolabeled substances include '*' to indicate label position)
2. The purity of the test substance (for radiolabeled substances include radiopurity and specific activity)
3. Solubility of the test material in water (include temperature and pH)
4. Reference additional studies that are presented to satisfy this data requirement, that use alternate radiolabeling and that are included in this summary package

C. **Soil description**

1. Description of test soil source (including country, state of origin, etc) for each soil used
2. Description test soil type (USDA classification)
3. Description of soil characteristics
    a. % sand, silt, clay
    b. % organic material
    c. pH
    d. Cation exchange capacity (meq/100 grams)
4. Comparison of foreign soil (if used), including soil characteristics (noted above) and microbial activity, to U.S. soils
5. Description of soil preparation including sieve size
6. Indicate other studies supporting this registration which use this soil

D. **Test Methodology**

1. Level of fortification
2. Description of treatment technique
3. Description of soil moisture content throughout study
4. Temperature range during experiment
5. Description of method used to initiate and maintain anaerobic conditions
6. Description of sampling intervals including time zero concentration: (indicate hr, day, weeks)
7. Description of volatility trap and analysis procedures (if used)
8. Description of extraction method for parent material and individual degradates
9. Description of extraction efficiency as percent of applied individually for parent and degradates
10. Description of analytical method including standards used and percent recovery
11. Description of storage conditions
12. Description of storage stability and results

E. **Reported Results**

1. Description of material balance at sampling intervals as percent of applied
2. Description of half-life estimation for parent
3. Description or graph of formation and decline of parent and degradates
4. Description of anaerobicity measurement (Eh) and results if measured.

F. **Discussion of Results**

162-3 Anaerobic Aquatic Metabolism

ACCEPTANCE CRITERIA

Does your study meet the following acceptance criteria?

1. ____ Test substance was the Technical Grade (TGAI) or a Pure Active Ingredient Radiolabeled (PAIRA).

2. ____ Radiopurity and specific activity of Active Ingredient (AI) (if radiolabeled).

3. ____ The positions of the AI radiolabeling were appropriate (if radiolabeled).

4. ____ Experiments were conducted with each respectively labelled ring (for compounds containing more than one ring structure).

5. ____ Water, sediment or soil were completely characterized, using the USDA classification system.

6. ____ Foreign soils or sediment (if any) were adequately compared with domestic (USA) soils/sediments.

7. ____ The maximum length of the study was one year.

8. ____ Anaerobic conditions were assured and maintained.

9. ____ Application rate was consistent with the sensitivity of the analytical method, so that degradates could be identified.

10. ____ Reported experimental temperature was held constant (±1°C) between 18 and 30° C.

11. ____ Sampling intervals for water and sediment were adequate.

12. ____ A reasonable attempt was made to identify the parent and all degradates [which exceeded 10% of application or 0.01 ppm (whichever is smaller)].

13. ____ The unextractable fraction was reasonable (i.e. a reasonable attempt was made -- perhaps with multiple solvent systems -- to extract metabolites/degradates).

14. ____ Half-life of parent was calculated.

15. ____ Patterns of formation and decline of major degradates were reported.

16. ____ Material balance was reasonable (>90% - <110%).

Criteria marked with a * are supplemental and may not be required for every study.

17.*____ Detection limits were reported.

18. ____ Appropriate analytical methods were provided.

Criteria marked with a * are supplemental and may not be required for every study.

162-3 Anaerobic Aquatic Metabolism

GUIDANCE FOR SUMMARIZING STUDIES

Items in summary should include the items discussed in Chapter 2 of this package and the specific items listed below.

A. **Summary of Conclusions**

B. **Test Material**

1. The chemical structure: (for radiolabeled substances include '*' to indicate label position)
2. The purity of the test substance (for radiolabeled substances include radiopurity and specific activity)
3. Solubility of the test material in water (include temperature and pH)
4. Reference additional studies that are presented to satisfy this date requirement, that use alternate radiolabeling and that are included in this summary package

C. **Test media**

1. Description of each test soil or sediment source (including country, state of origin, etc) for each soil used
2. Description test soil or sediment type (USDA classification)
3. Description of soil or sediment characteristics
    a. % sand, silt, clay
    b. % organic material
    c. pH
    d. Cation exchange capacity (meq/100 grams)
4. Comparison of foreign soil/sediment (if used), including soil/sediment characteristics (noted above) and microbial activity, to U.S. soils/sediments
5. Description of soil/sediment preparation including sieve size
6. Description of water source and characteristics (including pH, conductivity, hardness, etc) if available
7. Indicate other studies supporting this registration which use this soil/sediment

D. **Test Methodology**

1. Level of fortification
2. Description of treatment technique
3. Temperature range during experiment
4. Description of method used to initiate and maintain anaerobic conditions
5. Description of sampling intervals including time zero concentration: (indicate hr, day, weeks)
6. Description of volatility trap and analysis procedures (if used)
7. Description of extraction method for parent material and individual degradates in soil/sediment and water fractions
8. Description of extraction efficiency as percent of applied individually for parent and degradates
9. Description of analytical method including standards used and percent recovery
10. Description of storage conditions
11. Description of storage stability and results

E. **Reported Results**

1. Description of material balance at sampling intervals as percent of applied
2. Description of half-life estimation for parent
3. Description or graph of formation and decline of parent and degradates
4. Description of anaerobicity measurement (Eh) and results if measured.

F. **Discussion of Results**

162-4 Aerobic Aquatic Metabolism

ACCEPTANCE CRITERIA

Does your study meet the following acceptance criteria?

1. ____ Test substance was the Technical Grade (TGAI) or a Pure Active Ingredient Radiolabeled (PAIRA).

2. ____ Radiopurity and specific activity of Active Ingredient (AI)(if radiolabeled).

3. ____ The positions of the AI radiolabeling were appropriate (if radiolabeled).

4. ____ Experiments were conducted with each respectively labelled ring (for compounds containing more than one ring structure).

5.* ____ Water was adequately characterized.

6. ____ Foreign soils/sediment (if any) were adequately compared with domestic (USA) soils/sediments.

7. ____ Sediment was representative of the intended use site.

8. ____ Both aerobic and aquatic conditions were assured and maintained.

9. ____ Application rate was consistent with the sensitivity of the analytical method, so that degradates could be identified.

10. ____ Reported experimental temperature was held constant (±1°C) between 18 and 30°C.

11. ____ Sampling intervals were adequate over the 30 days of the study.

12. ____ A reasonable attempt was made to identify the parent and all degradates [which exceeded 10% of application or 0.01 ppm (whichever is smaller)].

13. ____ A reasonable attempt was made -- perhaps with multiple solvent systems -- to extract metabolites/degradates.

14. ____ Half-life of parent was calculated.

15. ____ Patterns of formation and decline of major degradates were reported.

16. ____ Material balance was reasonable (>90% - <110%)

Criteria marked with a * are supplemental and may not be required for every study.

17.*____ Detection limits were reported.

18. ____ Appropriate analytical methods were provided.

Criteria marked with a * are supplemental and may not be required for every study.

162-4 Aerobic Aquatic Metabolism

GUIDANCE FOR SUMMARIZING STUDIES

Items in summary should include the items discussed in Chapter 2 of this package and the specific items listed below.

A. **Summary of Conclusions**

B. **Test Material**

1. The chemical structure: (for radiolabeled substances include '*' to indicate label position)
2. The purity of the test substance (for radiolabeled substances include radiopurity and specific activity)
3. Solubility of the test material in water (include temperature and pH)
4. Reference additional studies that are presented to satisfy this date requirement, that use alternate radiolabeling and that are included in this summary package.

C. **Test Media**

1. Description of test soil/sediment source (including country, state of origin, etc) for each soil used
2. Description test soil/sediment type (USDA classification)
3. Description of soil/sediment characteristics
    a. % sand, silt, clay
    b. % organic material
    c. pH
    d. Cation exchange capacity (meq/100 grams)
4. Comparison of foreign soil/sediment (if used), including soil/sediment characteristics (noted above) and microbial activity, to U.S. soils/sediments
5. Description of soil/sediment preparation including sieve size
6. Description of water source and characteristics (including pH, conductivity, hardness, etc) if available
7. Indicate other studies supporting this registration which use this soil/sediment

D. Test Methodology

1. Level of fortification
2. Description of treatment technique
3. Temperature range during experiment
4. Description of method used to maintain aerobic conditions
5. Description of soil/sediment and water sampling intervals including time zero concentration: (indicate hr, day, weeks)
6. Description of volatility traps and analytical procedures (if used)
7. Description of extraction method for parent material and individual degradates in soil/sediment and water fractions
8. Description of extraction efficiency as percent of applied individually for parent and degradates
9. Description of analytical method including standards used and percent recovery
10. Description of storage conditions
11. Description of storage stability and results

E. Reported Results

1. Description of material balance at sampling intervals as percent of applied
2. Description of half-life estimation for parent
3. Description or graph of formation and decline of parent and degradates
4. Description of aerobicity measurement (Eh) and results if measured.

F. Discussion of Results

163-1 Leaching/Adsorption/Desorption

ACCEPTANCE CRITERIA

Does your study meet the following acceptance criteria?

1. ____ Testing method was Batch Equilibrium or Soil Column.

2. ____ Test substance was the Technical Grade (TGAI) or a Pure Active Ingredient Radiolabeled (PAIRA).

3. ____ Radiopurity and specific activity of Active Ingredient (AI) (if radiolabeled).

4. ____ The positions of the AI radiolabeling were appropriate (if radiolabeled).

5. ____ Experiments were conducted with each respectively labelled ring (for compounds containing more than one ring structure.

6. ____ At least 4 soils were used, which had pH's between 4 and 8.

7. ____ One soil had a %OM < 1%.

8. ____ One of the soils was the same type of soil used in the aerobic metabolism study.

9. ____ Soils were completely characterized using the USDA classification system.

10. ____ Soils were not sieved using a screen smaller than 2mm.

11.*____ Soil moisture was maintained at 75% of 1/3 bar during the aging process.

12. ____ Foreign soils (if any) were adequately compared with domestic (USA) soils.

13. ____ Test substance was added to the soil at the highest recommended label rate for a single application.

14.*____ Material balance was reasonable (>90% - <110%).

15. ____ Mobility of parent and all major degradates identified in the laboratory metabolism studies was determined during each column leaching study.

Criteria marked with a * are supplemental and may not be required for every study.

For SOIL TLC... (no longer recommended)

1. ____ Reference standards for degradates identified in the laboratory metabolism studies were used.
2. ____ R_f values were reported for parent and degradates.

For SOIL COLUMN...

1. ____ Elution volume was equivalent to 20" (50.8 cm times the cross-sectional area of the column).
2. ____ Column length was adequate.
3. ____ Distribution (identity and quantity) of major degradates/metabolites within the column (including eluate) was determined.

For AGED LEACHING...

1. ____ Test substance was aged for 30 days or one half-life (whichever is shorter).
2. ____ A reasonable attempt made to identify the parent and degradates.

For BATCH EQUILIBRIUM...

1. ____ Test substance was equilibrated at a minimum of 4 concentrations, with adequate time allowed for complete equilibration.
2. ____ 0.01N Ca^{++} solution was used.
3. ____ Appropriate analytical methods were provided.
4. ____ Detection limits were reported.
5. ____ K_{ads}, K_{des} and K_{oc} were reported.

Criteria marked with a * are supplemental and may not be required for every study.

163-1 Leaching/Adsorption/Desorption

GUIDANCE FOR SUMMARIZING STUDIES

Items in summary should include the items discussed in Chapter 2 of this package and the specific items listed below.

A. **Summary of Conclusions**

B. **Test Material**

1. The chemical structure: (for radiolabeled substances include '*' to indicate label position)

2. The purity of the test substance (for radiolabeled substances include radiopurity and specific activity)

3. Solubility of the test material in water (include temperature and pH)

4. Reference additional studies that are presented to satisfy this data requirement, that use alternate radiolabeling and that are included in this summary package.

C. **Descriptions of the Required Four Soils**

1. Description of test soil source (including country, state of origin, etc) for each soil used

2. Description test soil type (USDA classification)

3. Description of soil characteristics

   a. % sand, silt, clay

   b. % organic material

   c. pH

   d. Cation exchange capacity (meq/100 grams)

4. Comparison of foreign soil (if used), including soil characteristics (noted above) and microbial activity, to U.S. soils

5. Description of soil preparation including sieve size and sterilization technique (if used)

6. For aged residues, description of aerobic incubation conditions prior to leaching test

7. Indicate other studies supporting this registration which use this soil

D. Test Methodology

1. Batch equilibrium method
    - a. Levels of fortification
    - b. Description of equilibrating solution (e.g. 0.01N Ca ion solution)
    - c. Description of equilibration time and technique
    - d. Description of cosolvent, if used
    - e. Description of sampling intervals including time zero concentration: (indicate hr, day)
    - f. Description of analytical method for parent and degradates
2. Soil column
    - a. Description of column (dia. x length) and soil column preparation
    - b. Description of column equilibration, if any
    - c. Description of and volume of soil column eluate
    - d. Description of extraction method for parent material and individual degradates
    - e. Description of analytical method for parent and degradates
3. Soil Thin Layer Chromatography (TLC)
    - a. Description of TLC plate preparation
    - b. Description of test substance application technique

E. Reported Results

1. Batch equilibrium results
    - a. Description of material balance at sampling intervals as percent of applied
    - b. Description of K_d (and K_{oc}, if available) calculations and results

2. Soil column

   a. Description of material balance as percent of fortification levels

   b. Description of distribution curve of parent and degradates in 6 inch (15 cm) soil column segments and in the eluate

3. Soil TLC

   a. Description of material balance as percent of fortification levels

   b. Description of soil TLC R_f calculations and results according to mobility class of the parent and individual degradates

163-2 Laboratory Volatility

ACCEPTANCE CRITERIA

Does your study meet the following acceptance criteria?

1.*____ A greenhouse or field volatility study was provided as a substitute for this data requirement.

2. ____ A typical End Use Product (EP) was used, or an adequate explanation provided to justify the alternative chosen.

3. ____ Radiopurity and specific activity of Active Ingredient (AI) (if radiolabeled).

4. ____ The positions of the AI radiolabeling were appropriate (if radiolabeled).

5. ____ Experiments were conducted with each respectively labelled ring (for compounds containing more than one ring structure).

6. ____ Soils were completely characterized, using the USDA classification system.

7. ____ Foreign soils (if any) were adequately compared with domestic (USA) soils.

8. ____ Test substance was added to the soil at the highest recommended label rate for a single application.

9. ____ Sampling intervals were adequate.

10. ____ The decline of the AI was clearly established.

11. ____ Material balance was reasonable (>90% - <110%)

12. ____ Trapping efficiencies were reasonable.

13. ____ Reported experimental temperature was held constant (±1°C) between 18 and 30°C.

14.*____ Volatility was reported in the correct units ($\mu g/cm^2/hr$).

15. ____ The concentration of the AI in air was measured.

16.*____ The concentration of AI in air was reported in the correct units (ng/m^3 or $\mu g/m^3$).

17.*____ The vapor pressure was reported in the correct units (Torr, or mm Hg), including the temperature at which it was determined.

18. ____ Appropriate analytical methods were provided.

Criteria marked with a * are supplemental and may not be required for every study.

19.*____ Detection limits were reported.

Criteria marked with a * are supplemental and may not be required for every study.

163-2 Laboratory Volatility

GUIDANCE FOR SUMMARIZING STUDIES

Items in summary should include the items discussed in Chapter 2 of this package and the specific items listed below.

A. **Summary of Conclusions**

B. **Test Material**

1. The chemical structure: (for radiolabeled substances include '*' to indicate radiolabel position, if radioactive compound is used)
2. The purity of the test substance (for radiolabeled substances include radiopurity and specific activity, if radioactive compound is used)
3. Vapor pressure at 25°C and water solubility of the test material (include temperature and pH)
4. Reference additional studies that are presented to satisfy this data requirement, that use alternate radiolabeling and that are included in this summary package

C. **Soil Description**

1. Description of test soil source (including country, state of origin, etc) for each soil used
2. Description test soil type (USDA classification)
3. Description of soil characteristics
    a. % sand, silt, clay
    b. % organic material
    c. pH
    d. Cation exchange capacity (meq/100 grams)
4. Comparison of foreign soil (if used), including soil characteristics (noted above) and microbial activity, to U.S. soils
5. Description of soil preparation including sieve size and sterilization technique (if used)
6. Indicate other studies supporting this registration which use this soil

D. Test Methodology

1. Level of fortification
2. Description of treatment technique and laboratory test equipment
3. Description of soil moisture content throughout study
4. Temperature range during experiment
5. Description of method used to maintain aerobic soil conditions and collect air samples
6. Description of sampling intervals including time zero concentration: (indicate hr, day, weeks)
7. Description of volatility traps and analysis procedures (if used)
8. Description of analytical method including standards used and percent recovery

E. Reported Results

1. Description of calculations for volatility expressed as $\mu g/cm^2$/hour, air concentration expressed as $\mu g/m^3$ of mg/m^3 and vapor pressure expressed as Torr (or other equivalent units)
2. Description of results based on calculations

F. Discussion of Results

163-3 Field Volatility

ACCEPTANCE CRITERIA

Does your study meet the following acceptance criteria?

1. ____ The study was conducted domestically (USA).

2. ____ A typical End Use Product (EP) was used, or an adequate explanation provided to justify the alternative chosen.

3. ____ Test substance was added to the soil at the highest recommended label rate for a single application.

4. ____ The test site (including soil type) was typical of actual use; soil was adequately characterized using the USDA classification system.

5. ____ The site used for this study was clearly shown to have no previous use history involving this (or closely related) compound (AI).

6. ____ Environmental conditions were typical, and adequately described.

7. ____ Sampling intervals were adequate.

8. ____ The decline of the AI was clearly established.

9.*____ Volatility was reported in the correct units ($\mu g/cm^2/hr$).

10. ____ The concentration of the AI in air was measured.

11.*____ The concentration of AI in air was reported in the correct units (ng/m^3 or $\mu g/m^3$).

12.*____ The vapor pressure was reported in the correct units (Torr, or mm Hg), including the temperature range over which it was determined.

13. ____ Appropriate analytical methods were provided.

14.*____ Detection limits were reported.

15. ____ A storage stability study was conducted using either spiked field or spiked laboratory samples to determine the stability of samples under typical storage conditions.

Criteria marked with a * are supplemental and may not be required for every study.

163-3 Field Volatility

GUIDANCE FOR SUMMARIZING STUDIES

Items in summary should include the items discussed in Chapter 2 of this package and the specific items listed below.

A. **Summary of Conclusions**

B. **Test Material**

1. The chemical structure: (for radiolabeled substances include '*' to indicate label position)
2. The purity of the test substance (for radiolabeled substances include radiopurity and specific activity)
3. Volatility and water solubility of the test material (include temperature range and pH)
4. Reference additional studies that are presented to satisfy this data requirement, that use alternate radiolabeling and that are included in this summary package.

C. **Test Site**

1. Location
2. Description of test soil type (USDA classification)
3. Description of soil characteristics
    a. % sand, silt, clay
    b. % organic material
    c. pH
    d. Cation exchange capacity (meq/100 grams)
4. Indicate other studies supporting this registration which use this soil
5. Description of environmental conditions during test

D. **Test Methodology**

1. Application method/rate
2. Description of method used to collect air samples
3. Description of sampling intervals including time zero concentration: (indicate hr, day, weeks)

4. Description of volatility traps and sampling procedures

5. Description of analytical method including standards used and percent recovery

E. **Reported Results**

1. Description of calculations for volatility expressed as $\mu g/cm^2/hour$, air concentration expressed as $\mu g/m^3$ of mg/m^3 and vapor pressure expressed as torr (or other equivalent units)

2. Description of results based on calculations

3. Description of climatic conditions during study

F. **Discussion of Results**

164-1 Terrestrial Field Dissipation

ACCEPTANCE CRITERIA

Does your study meet the following acceptance criteria?

1. ____ The study was conducted domestically (USA).

2. ____ The site used for this study was clearly shown to have no previous use history involving this (or closely related) compound (AI) or was clearly shown to contain no background residues or analytical interferences.

3. ____ The test site (including soil type) was typical of the proposed use pattern. If intended application is to turf, vineyard, orchard or other similar use patterns, a bare-ground plot is also required.

4. ____ Study was conducted under typical use conditions.

5. ____ At least 2 sites were used, either in 2 different areas representative of the intended usage, or in 1-2 similar sites for limited use patterns.

6. ____ A typical End Use Product (EP) was used, or an adequate explanation provided to justify the alternative chosen.

7. ____ Test substance was added to the soil at the highest recommended label rate for a single application or the highest recommended rate for each application or multiple application.

8.*____ Specifics were provided regarding time of year, meteorological conditions during exposure, etc.

9. ____ Soil was adequately characterized using the USDA classification system.

10. ____ Samples were selected randomly.

11. ____ The soil cores were of sufficient number with minimal compositing for each sampling time to define the heterogeneity of the soil and pesticide degradation. A minimum of 15 soil cores with a minimum of three composites is recommended per plot

12. ____ Sampling was done to a sufficient depth to define leaching (90 cm) at all sampling intervals, or a rationale was given for not doing so.

13. ____ Monitoring adequately detected all major degradates identified in the aerobic and/or anaerobic metabolism studies.

Criteria marked with a * are supplemental and may not be required for every study.

14. ____ Study was conducted until patterns of decline of parent and patterns of formation/decline of degradates were established.

15.*____ The depth to the water table was reported.

16. ____ Sampling intervals were adequate to define $t_{1/2}$ under field conditions.

17. ____ Sampling intervals were adequate to track any vertical movement associated with rainfall.

18. ____ Appropriate analytical methods were provided.

19. ____ Half-life of parent and major degradates under field conditions was determined.

20. ____ A storage stability study was conducted using either spiked field or spiked laboratory samples to determine the stability of samples under typical lab storage conditions.

21. ____ The test duration following a single event was consistent with the following:
    Field and vegetable crop uses: 18 months
    Orchard crop and pastureland uses: 12 months
    Domestic outdoor, park, ornamental, and turf uses: 4 months
    Rights of way, shelter belts and related uses: 2 months

22. ____ Detection limits were reported

23. ____ A reasonable attempt was made to identify the parent and all degradates [which exceeded 10% (yield) of the initial concentration of the AI or 0.01 ppm (whichever is smaller)].

Criteria marked with a * are supplemental and may not be required for every study.

164-1 Terrestrial Field Dissipation

GUIDANCE FOR SUMMARIZING STUDIES

Items in summary should include the items discussed in Chapter 2 of this package and the specific items listed below.

A. Summary of Conclusions

B. Test Material

1. The chemical structure: (for radiolabeled substances include '*' to indicate label position)
2. The purity of the test substance (for radiolabeled substances include radiopurity and specific activity)
3. Solubility of the test material in water (include temperature and pH)
4. Reference additional studies that are presented to satisfy this data requirement, that use alternate radiolabeling and that are included in this summary package.

C. Description of the required two test sites

1. Identify each test location (including state, county etc) for each test site used
2. Description test soils type (USDA classification)
3. Description of soil characteristics
    a. % sand, silt, clay
    b. % organic material
    c. pH
    d. Cation exchange capacity (meq/100 grams)
4. Indicate other studies supporting this registration which use this soil
5. Description of environmental conditions during test
6. Description of pesticide use history of site, if available
7. Topographical description of test sites.

D. **Test Methodology**

1. Description of application method/rate and other field test data

2. Description of sampling methodology and sampling intervals including pre-application, date of application and immediate post-application (indicate hr, day, weeks)

3. Description of analytical method of soil cores including standards used and percent recovery

4. Description of soil profile and depth to water table, if available

5. Description of sample storage conditions

6. Description of storage stability and results

7. Description of climatic conditions, including amount of rainfall or irrigation water, during test period

E. **Reported Results**

1. Description of half-life calculation for parent and degradates

2. Description or graph of formation and decline of parent and degradates

3. Description of leaching movement, if observed

F. **Discussion of Results**

164-2 Aquatic Field Dissipation

ACCEPTANCE CRITERIA

Does your study meet the following acceptance criteria?

1. ____ The study was conducted domestically (USA).

2. ____ A typical End Use Product (EP) was used, or an adequate explanation provided to justify the alternative chosen.

3. ____ At least 2 sites were used, either in 2 different areas representative of the intended usage, or in 1 to 2 similar sites for limited use patterns.

4. ____ Test substance was added to the soil at the highest recommended label rate for a single application or the highest recommended rate for multiple applications.

5. ____ The test site (including soil type) was typical of the proposed use pattern.

6. ____ The site used for this study was clearly demonstrated to have no previous use history involving this (or closely related) compound (AI) or was clearly shown to contain no background residues or analytical interferences.

7. ____ Study was conducted under typical use conditions.

8.*____ Specifics were provided regarding time of year, meteorological conditions during exposure, etc.

9. ____ Soil and sediments (if required) were adequately characterized using the USDA classification system.

10. ____ Soil, water and sediments (if required) were analyzed.

11. ____ Samples were selected randomly.

12. ____ The soil cores were of sufficient number with minimal compositing for each sampling time to define the heterogeneity of the soil and pesticide degradation. A minimum of 15 soil cores with a minimum of three composites is recommended per plot.

13. ____ Soil sampling was done to a depth of at least 15 cm.

14. ____ Sediment sampling was done to a depth of at least 5 cm.

15. ____ Sampling intervals were adequate to define $t_{1/2}$ of parent under field conditions.

Criteria marked with a * are supplemental and may not be required for every study.

16. ____ The test duration following a single event was consistent with the following table:

water		1 month
sediments	(for Aquatic non-crop uses)	6 months
	(for multiple application)	9 months
soil	(for Aquatic non-crop uses)	6 months
	(for multiple applications)	9 months

17. ____ Appropriate analytical methods were provided.

18.*____ Detection limits were reported.

19. ____ A reasonable attempt was made to identify the parent and all degradates [which exceed 10% (yield) of the initial concentration of the AI or 0.01 ppm (whichever is smaller)].

20. ____ Half-life of parent and major degradates under field conditions was determined.

21. ____ A storage stability study was conducted using either spiked field or spiked laboratory samples to determine the stability of samples under typical storage conditions.

Criteria marked with a * are supplemental and may not be required for every study.

164-2 Aquatic Field Dissipation

GUIDANCE FOR SUMMARIZING STUDIES

Items in summary should include the items discussed in Chapter 2 of this package and the specific items listed below.

A. Summary of Conclusions

B. Test Material

1. The chemical structure: (for radiolabeled substances include '*' to indicate label position)
2. The purity of the test substance (for radiolabeled substances include radiopurity and specific activity)
3. Solubility of the test material in water (include temperature and pH)
4. Reference additional studies that are presented to satisfy this data requirement, that use alternate radiolabeling and that are included in this summary package

C. Description of the Required Two Test Sites

1. Identify each test location (including state, county etc) for each test site used
2. Description test soil and sediment type (USDA classification) and water characteristics (pH, hardness, sediment load, etc)
3. Description of soil and sediment characteristics
    a. % sand, silt, clay
    b. % organic material
    c. pH
    d. Cation exchange capacity (meq/100 grams)
4. Indicate other studies supporting this registration which use this soil and sediment
5. Description of environmental conditions during test
6. Description of pesticide use history of site, if available
7. Topographical description of test sites.

D. **Test Methodology**

1. Description of application method/rate and other field test data
2. Description of sampling methodology and sampling intervals including pre-application, date of application and immediate post-application to maximum test duration (indicate hr, day, weeks)
3. Description of analytical method of soil/sediment and water samples including standards used and percent recovery
4. Description of sample storage conditions
5. Description of storage stability and results
6. Description of climatic conditions, including amount of rainfall or flood water, during test period
7. Description of flow data in terms of volume or linear flow

E. **Reported Results**

1. Description of half-life calculation for parent and degradates
2. Description or graph of formation and decline of parent and degradates

F. **Discussion of Results**

164-3 Forest Field Dissipation

ACCEPTANCE CRITERIA

Does your study meet the following acceptance criteria?

1. ____ The study was conducted domestically (USA).

2. ____ A typical End Use Product (EP) was used, or an adequate explanation provided to justify the alternative chosen.

3. ____ Test substance was applied at the highest recommended label rate for a single application or the highest recommended rate for multiple applications.

4. ____ Application rate was confirmed by immediate post-application sampling.

5. ____ The method of application was consistent with label requirements/recommendations.

6. ____ The test site (including soil type) was typical of the proposed use pattern.

7. ____ The site used for this study was clearly demonstrated to have no previous use history involving this (or closely related) compound (AI) or was clearly shown to contain no background residues or analytical interferences.

8. ____ Soil and sediments were adequately characterized using the USDA classification system.

9. ____ Samples were taken of each of the following components:

   - foliage (if foliarly applied)
   - leaf litter
   - soil under leaf litter
   - exposed soil
   - standing (pond) water
   - moving (stream) water
   - sediments (ponds)
   - sediments (stream)

10. ____ The correct sampling intervals were used for...

   - foliage[a]
   - leaf litter[a]
   - soil under leaf litter[a]
   - exposed soil[a]
   - standing (pond) water[b]
   - moving (stream) water[b]

Criteria marked with a * are supplemental and may not be required for every study.

- sediments (pond)[b]
- sediments (stream)[b]

11. ____ Samples were taken for an adequate duration for...

- foliage (12 mo[c])
- leaf litter (12 mo[c])
- soil under leaf litter (12 mo[c])
- exposed soil (12 mo[c])
- standing (pond) water (1 mo[c])
- moving (stream) water (1mo[c])
- sediments (pond and stream) (6 mo[c])

12. ____ Monitoring adequately detected the major degradates identified in the aerobic and/or anaerobic metabolism studies.

13. ____ Half-life of parent and major degradates under field conditions was determined.

14. ____ Specifics were provided regarding time of year, meteorological conditions during exposure, etc.

15. ____ Appropriate analytical methods were provided.

16.*____ Detection limits were reported.

17. ____ A storage stability study was conducted using either spiked field or spiked laboratory samples to determine the stability of samples under typical lab storage conditions.

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[a] pre-application, day 0, and at least 3 samples within the first week for each single or multiple application.

[b] pre-application, day 0, and at least 1 sample within the first week for each single or multiple application.

[c] or until establishment of patterns of decline of parent, and formation and decline of degradates.

Criteria marked with a * are supplemental and may not be required for every study.

164-3 Forest Field Dissipation

GUIDANCE FOR SUMMARIZING STUDIES

Items in summary should include the items discussed in Chapter 2 of this package and the specific items listed below.

A. **Summary of Conclusions**

B. **Test Material**

1. The chemical structure of the test substance
2. The purity of the test substance and pounds AI per acre applied
3. Solubility of the test material in water (include temperature and pH)
4. Reference additional studies that are presented to satisfy this data requirement and that are included in this summary package

C. **Description of the Test Site**

1. Identify test location (including country, state of origin, etc)
2. Description test soil type (USDA classification)
3. Description of soil characteristics for exposed soil areas
    a. % sand, silt, clay
    b. % organic material
    c. pH
    d. Cation exchange capacity (meq/100 grams)
4. Indicate other forest dissipation studies supporting this registration
5. Description of climatic conditions during test
6. Description of pesticide use history of site, if available
7. Topographical description of test site

D. **Test Methodology**

1. Description of application method/rate and other field test data

2. Description of sampling methodology for the various environmental components (e.g. foliage, leaf litter, covered and exposed soil, standing and moving water and sediments)

3. Description of sampling intervals including pre-application, date of application and immediate post-application for the test duration (indicate hr, day, weeks)

4. Description of methods of analysis of the various environmental components of the study including standards used and percent recovery

5. Description of sample storage conditions

6. Description of storage stability and results

7. Description of climatic conditions, including amount of rainfall or irrigation water, during test period

E. **Reported Results**

1. Description of half-life calculation for parent and degradates for each substrate analyzed (e.g. foliage, leaf litter, etc)

2. Description or graph of formation and decline of parent and degradates

3. Description of other field test data

F. **Discussion of Results**

164-5 Long-Term Soil Dissipation

ACCEPTANCE CRITERIA

Does your study meet the following acceptance criteria?

1. ____ The study was conducted domestically (USA).

2. ____ The site used for this study was clearly shown to have no previous use history involving this (or closely related) compound (AI) or was clearly shown to contain no background residues or analytical interferences.

3. ____ The test site (including soil type) was typical of the proposed use pattern. If intended application is to turf, vineyard, orchard or other similar use patterns, a bare-ground plot is also required.

4. ____ Study was conducted under typical use conditions.

5. ____ At least 2 sites were used, either in 2 different areas representative of the intended usage, or in 1-2 similar sites for limited use patterns.

6. ____ A typical End Use Product (EP) was used, or an adequate explanation provided to justify the alternative chosen.

7. ____ Test substance was added to the soil at the highest recommended label rate for a single application or the highest recommended rate for multiple applications.

8.*____ Specifics were provided regarding time of year, meteorological conditions during exposure etc.

9. ____ Soil was adequately characterized using the USDA classification system.

10. ____ Samples were selected randomly.

11. ____ The soil cores were of sufficient number with minimal compositing for each sampling time to define the heterogeneity of the soil and pesticide degradation. A minimum of 15 soil cores with a minimum of three composites is recommended per plot.

12. ____ Sampling was done to a sufficient depth to define leaching (90 cm) at all sampling intervals, or a rationale was given for not doing so.

13. ____ Monitoring adequately detected all major degradates identified in the aerobic and/or anaerobic metabolism studies.

Criteria marked with a * are supplemental and may not be required for every study.

14. ____ Study was conducted until patterns of decline of parent and patterns of formation/decline of degradates were established.

15.*____ The depth to the water table was reported.

16. ____ Sampling intervals were adequate to define $t_{1/2}$ under field conditions.

17. ____ Sampling intervals were adequate to track any vertical movement associated with rainfall.

18. ____ Appropriate analytical methods were provided.

19. ____ Half-life of parent and major degradates under field conditions was determined.

20. ____ A storage stability study was conducted using either spiked field or spiked laboratory samples to determine the stability of samples under typical storage conditions.

Criteria marked with a * are supplemental and may not be required for every study.

164-5 Long-Term Soil Dissipation

GUIDANCE FOR SUMMARIZING STUDIES

Items in summary should include the items discussed in Chapter 2 of this package and the specific items listed below.

A. **Summary of Conclusions**

B. **Test Material**

1. The chemical structure of the test substance
2. The purity of the test substance and pounds AI per acre applied
3. Reference additional studies that are presented to satisfy this data requirement and that are included in this summary package

C. **Description of the Test Sites**

1. Identify each test location (including state, county, etc.) for each test site used
2. Description test soils type (USDA classification)
3. Description of soil characteristics
    a. % sand, silt, clay
    b. % organic material
    c. pH
    d. Cation exchange capacity (meq/100 grams)
4. Indicate other studies supporting this registration which use this soil
5. Description of environmental conditions during test
6. Description of pesticide use history of site, if available
7. Topographical description of test sites.

D. Test Methodology

1. Description of application method/rate and other field test data
2. Description of sampling methodology and sampling intervals for the test duration application, date of application and immediate post-application: (indicate hour, day, week)
3. Description of analytical method of soil cores including standards used and percent recovery
4. Description of soil profile and depth to water table, if available
5. Description of sample storage conditions
6. Description of storage stability and results
7. Description of climatic conditions, including amount of rainfall or irrigation water, during test period

E. Reported Results

1. Description of half-life calculation for parent and degradates
2. Description or graph of formation and decline of parent and degradates
3. Description of leaching movement, if observed

F. Discussion of Results

165-1 Confined Rotational Crops

ACCEPTANCE CRITERIA

Does your study meet the following acceptance criteria?

1. ____ Test substance was added to the soil at the highest recommended label rate for a single application or the highest recommended rate for multiple applications.

2. ____ Test substance was a Pure Active Ingredient Radiolabeled (PAIRA).

3. ____ Radiopurity and specific activity of Active Ingredient (AI) (if radiolabeled).

4. ____ The positions of the AI radiolabeling were appropriate (if radiolabeled).

5. ____ Experiments were conducted with each respectively labeled ring (for compounds containing more than one ring structure).

6. ____ A sandy loam soil was used, or another type was justified.

7. ____ Soil was adequately characterized using the USDA classification system.

8. ____ Rainfall/irrigation data were provided (if study was outdoor-small plot).

9. ____ All three crop groupings were used (small grain, leafy vegetable, root crop).

10. ____ Representative crops were planted at appropriate soil aging intervals (eg. 30, 120, 210 and/or 360 days).

11. ____ Analyses were performed on appropriate plant parts, with adequate residue characterization.

12. ____ The extraction scheme was adequately described, including all methodology.

13.*____ Material balance was reasonable (>90% - <110%).

14.*____ Soil analyzed at the appropriate intervals, especially on day 0 (pre/post application, and at the time of planting each crop).

15. ____ Appropriate analytical methods were provided.

16.*____ Detection limits were reported.

17. ____ Extent of uptake of residues under laboratory conditions (including identity and concentration of parent and/or major degradates) was clearly demonstrated.

Criteria marked with a * are supplemental and may not be required for every study.

165-1 Confined Rotational Crops

GUIDANCE FOR SUMMARIZING STUDIES

Items in summary should include the items discussed in Chapter 2 of this package and the specific items listed below.

A. **Summary of Conclusions**

B. **Test Material**

1. The chemical structure: (for radiolabeled substances include '*' to indicate label position)
2. The purity of the test substance (for radiolabeled substances include radiopurity and specific activity)
3. Solubility of the test material in water (include temperature and pH)
4. Reference additional studies that are presented to satisfy this data requirement, that use alternate radiolabeling and that are included in this summary package

C. **Test media**

1. Description of test soil (sandy loam) source or test site (including country, state of origin, etc)
2. Description of soil characteristics
    a. % sand, silt, clay
    b. % organic material
    c. pH
    d. Cation exchange capacity (meq/100 grams)
3. Comparison of foreign soil (if used), including soil characteristics (noted above) and microbial activity, to U.S. soils
4. Description of soil preparation including sieve size
5. Indicate other studies supporting this registration which use this soil

D. **Test Methodology**

1. Description of application method/rate
2. Description of other test parameters (e.g. aging periods prior to rotational crop planting, identity of rotational crops, time from application to planting and to harvest of rotational crops, etc)

3. Description of sampling methodology and sampling intervals including pre-application, date of application and immediate post-application: (indicate hr, day, weeks)

4. Description of analytical methods of soil and rotational crop samples including standards used and percent recovery

5. Description of sample storage conditions

6. Description of storage stability and results

7. Description of environmental conditions, including amount of rainfall or irrigation water, during test period

E. **Reported Results**

1. Description of residues including parent and degradates in soil of each sampling interval

2. Description and results of half-life calculation for parent and degradates in soil, if available

3. Description and amounts of significant residues in rotational crops at each sampling interval including immature (if consumed by domestic animals or humans) and mature plant stages

F. **Discussion of Results**

165-2 Field Rotational Crops

ACCEPTANCE CRITERIA

Does your study meet the following acceptance criteria?

1. ____ The study was conducted domestically (USA).

2. ____ A typical End Use Product (EP) was used, or an adequate explanation provided to justify the alternative chosen.

3. ____ Test substance was added to the soil at the highest recommended label rate for a single application (as confirmed by immediate post-application sampling) or the highest recommended rate for multiple applications.

4. ____ Test substance was added to the soil consistent with label recommendations/requirements.

5. ____ At least 2 sites were used, either in 2 different areas representative of the intended usage, or in 1-2 similar sites for limited use patterns.

6. ____ The appropriate degradates/metabolites were adequately detected/quantified as indicated in the confined rotational crop study.

7. ____ One of the soils was the same type as in the confined study.

8. ____ Soil was adequately characterized using the USDA classification system.

9. ____ The test site (including soil type) was typical of the proposed use pattern.

10. ____ The site used for this study was clearly demonstrated to have no previous use history involving this (or closely related) compound (AI).

11. ____ Specifics were provided regarding time of year, meteorological conditions during exposure, etc.

12. ____ All three crop groupings were used (small grain, leafy vegetable, root crop.)

13. ____ Representative crops were planted at appropriate soil aging intervals (eg. 30, 120, 210, and/or 360 days).

14. ____ Analyses were performed on appropriate plant parts, with adequate residue characterization.

15. ____ The extraction scheme was adequately described including all methodology.

Criteria marked with a * are supplemental and may not be required for every study.

16. ____ Soil analyzed at the appropriate intervals, especially on day 0 (pre/post application, and at the time of planting each crop).

17. ____ Appropriate analytical methods were provided.

18.*____ Detection limits were reported.

19. ____ Extent of uptake of residues under field conditions (including identity and concentration of parent and/or major degradates) was clearly demonstrated.

20. ____ A storage stability study was conducted using either spiked field or spiked laboratory samples to determine the stability of samples under typical storage conditions.

Criteria marked with a * are supplemental and may not be required for every study.

165-2 Field Rotational Crops

GUIDANCE FOR SUMMARIZING STUDIES

Items in summary should include the items discussed in Chapter 2 of this package and the specific items listed below.

A. **Summary of Conclusions**

B. **Test Material**

1. The chemical structure of the test compound
2. The purity of the test substance and pounds AI per acre applied
3. Solubility of the test material in water (include temperature and pH)
4. Reference additional studies that are presented to satisfy this data requirement and that are included in this summary package

C. **Description of the Required Two Test Sites**

1. Identify each test location (including state, county etc) for each test site used
2. Description of test soil types (USDA classification)
3. Description of soil characteristics
    a. % sand, silt, clay
    b. % organic material
    c. pH
    d. Cation exchange capacity (meq/100 grams)
4. Indicate other studies supporting this registration which use this soil
5. Description of environmental conditions during test
6. Description of pesticide use history of site, if available
7. Topographical description of test sites.

D. **Test Methodology**

1. Description of application method/rate

2. Description of other test parameters (e.g. aging periods prior to rotational crop planting, identity of rotational crops, time from application to planting and to harvest of rotational crops, etc)

3. Description of sampling methodology and sampling intervals including pre-application, date of application and immediate post-application: (indicate hr, day, weeks)

4. Description of analytical methods of soil and rotational crop samples including standards used and percent recovery

5. Description of sample storage conditions

6. Description of storage stability and results

7. Description of climatic conditions, including amount of rainfall or irrigation water, during test period

E. **Reported Results**

1. Description of residues including parent and degradates in soil of each sampling interval

2. Description and results of half-life calculation for parent and degradates in soil, if available

3. Description and amounts of significant residues in rotational crops at each sampling interval including immature (if consumed by domestic animals or humans) and mature plant stages

F. **Discussion of Results**

165-3 Accumulation in Irrigated Crops

ACCEPTANCE CRITERIA

Does your study meet the following acceptance criteria?

1. ____ The study was conducted domestically (USA).

2. ____ A typical End Use Product (EP) was used, or an adequate explanation provided to justify the alternative chosen.

3. ____ Test substance was added to the soil at the highest recommended label rate for a single application (as confirmed by immediate post-application sampling).

4. ____ Test substance was added to the soil consistent with label recommendations/requirements.

5. ____ At least 2 sites were used, either in 2 different areas representative of the intended usage, or in 1-2 similar sites for limited use patterns.

6. ____ The site used for this study was clearly demonstrated to have no previous use history involving this (or closely related) compound (AI) or was clearly shown to contain no background residues or analytical interferences..

7. ____ Analyses were performed on appropriate plant parts, with adequate residue characterization.

8. ____ The extraction scheme was adequately described, including all methodology.

9. ____ The appropriate degradates/metabolites were adequately detected/quantified as indicated in the confined rotational crop study.

10. ____ Soil was adequately characterized using the USDA classification system.

11. ____ The test site (including soil type) was typical of the proposed use pattern.

12. ____ Specifics were provided regarding time of year, meteorological conditions during exposure, etc.

13. ____ Soil analyzed at the appropriate intervals, especially on day 0 (pre/post application, and at the time of planting each crop).

14. ____ Irrigation water was analyzed.

15. ____ Crops were irrigated at the highest rate allowable following good agricultural practices.

16. ____ All three crop groupings were used (small grain, leafy vegetable, root crop).

Criteria marked with a * are supplemental and may not be required for every study.

17. ____ Appropriate analytical methods were provided.

18.*____ Detection limits were reported.

19. ____ Extent of uptake of residues under field conditions (including identity and concentration of parent and/or major degradates) was clearly demonstrated.

20. ____ A storage stability study was conducted using either spiked field or spiked laboratory samples to determine the stability of samples under typical storage conditions.

Criteria marked with a * are supplemental and may not be required for every study.

165-3 Accumulation in Irrigated Crops

GUIDANCE FOR SUMMARIZING STUDIES

Items in summary should include the items discussed in Chapter 2 of this package and the specific items listed below.

A. **Summary of Conclusions**

B. **Test Material**

1. The chemical structure of the test substance
2. The purity of the test substance and pounds AI per acre applied
3. Solubility of the test material in water (include temperature and pH)
4. Reference additional studies that are presented to satisfy this data requirement and that are included in this summary package

C. **Description of the Required Two Test Sites**

1. Identify each test location (including state, county etc) for each test site used
2. Description of test soil types (USDA classification) and water characteristics of the irrigation water (pH, hardness, sediment load, etc)
3. Description of soil characteristics
    a. % sand, silt, clay
    b. % organic material
    c. pH
    d. Cation exchange capacity (meq/100 grams)
4. Indicate other studies supporting this registration which use this soil
5. Description of environmental conditions during test
6. Description of pesticide use history of site, if available
7. Topographical description of test sites.

D. Test Methodology

1. Description of application method/rate to irrigation water
2. Description of other test parameters (e.g. identity of irrigated crops, time from water treatment to irrigation and to harvest of irrigated crops, flow rate and amount of irrigation water applied, etc)
3. Description of sampling methodology and sampling intervals (i.e. hr, day, weeks)
4. Description of methods of analysis of soil and irrigated crop samples including standards used and percent recovery
5. Description of sample storage conditions
6. Description of storage stability and results
7. Description of climatic conditions, including amount of rainfall or irrigation water, during test period

E. Reported Results

1. Description of residues including parent and degradates in soil of each sampling interval
2. Description and results of half-life calculation for parent and degradates in soil, if available
3. Description and amounts of significant residues in irrigated crops at each sampling interval including immature and mature plant stages

F. Discussion of Results

165-4 Bioaccumulation in Fish

ACCEPTANCE CRITERIA

Does your study meet the following acceptance criteria?

1. ____ Test substance was the Technical Grade (TGAI) or a Pure Active Ingredient Radiolabeled (PAIRA).
2. ____ Radiopurity and specific activity of Active Ingredient (AI) (if radiolabeled).
3. ____ The positions of the AI radiolabeling were appropriate (if radiolabeled).
4. ____ Experiments were conducted with each respectively labelled ring (for compounds containing more than one ring structure).
5. ____ The correct fish species was used (Bluegill Sunfish or Channel Catfish are preferred).
6. ____ Study was a flow-through type (not static).
7. ____ The pesticide concentration in the water was reasonably constant, and did not exceed 1/10 the 96 hr LC_{50}.
8. *____ A control group was used.
9. ____ Fish were exposed for about 28 days, or until an accumulation plateau was reached.
10. ____ Fish were depurated for about 14 days.
11. ____ Water was sampled at appropriate intervals.
12. ____ Fish tissues (edible vs. viscera) were appropriately analyzed at the various stages of accumulation and depuration.
13. ____ Extractable residues which exceeded 50 ppb were adequately identified.
14. ____ The extraction scheme was clearly described, including all methodology.
15. ____ Test conditions were adequately described.
16. ____ Pesticide concentrations in H_2O/fish were adequately reported.
17. ____ The level of degradates in the water was not unreasonably high.
18. ____ Appropriate analytical methods were provided.

Criteria marked with a * are supplemental and may not be required for every study.

19.*____ Detection limits were reported.

20. ____ Raw data in support of the Final Report are available.

Criteria marked with a * are supplemental and may not be required for every study.

165-4 Bioaccumulation in Fish

GUIDANCE FOR SUMMARIZING STUDIES

Items in summary should include the items discussed in Chapter 2 of this package and the specific items listed below.

A. Summary of Conclusions

B. Test Material

1. The chemical structure: (for radiolabeled substances include '*' to indicate label position)

2. The purity of the test substance (for radiolabeled substances include radiopurity and specific activity)

3. Solubility of the test material in water (include temperature and pH)

4. Reference additional studies that are presented to satisfy this data requirement, that may or may not use alternate radiolabeling and that are included in this summary package

C. Test Methodology

1. Identity and description (weight and length) of fish species

2. Description of study design and pre-exposure equilibration and exposure test conditions

3. Description of water source and characteristics (including pH, conductivity, hardness, dissolved oxygen, etc.)

4. Description of water and fish sampling intervals including exposure and depuration periods

5. Description of analytical methods for water and fish residues including extraction efficiency and percent recovery

E. Reported Results

1. Description of residues in water and fish tissues (whole body, edible and non-edible tissues) during the exposure period and in fish tissues during depuration period.

2. Description of fish bioconcentration calculations and bioconcentration factors for fish uptake (whole body, edible and non-edible tissues) at each sampling period

3. Description of sample storage conditions prior to analysis

4. Description of sample storage stability study and results

F. Discussion of Results

165-5 Bioaccumulation in Aquatic Non-Target Organisms

ACCEPTANCE CRITERIA

Does your study meet the following acceptance criteria?

1. ____ The study was conducted domestically (USA).

2. ____ A typical End Use Product (EP) was used, or an adequate explanation provided to justify the alternative chosen.

3. ____ Application was appropriate to the intended use pattern.

4. ____ The site which was used for this study clearly shown to have no previous use history involving this (or closely related) compound (AI) or was clearly shown to contain no background residues or analytical interferences.

5. ____ Fish from bottom, middle and surface feeding patterns were analyzed.

6. ____ Fish were adequately described as to species, size, etc.

7. ____ Test conditions were adequately described.

8. ____ Water/fish were both analyzed at appropriate intervals.

9. ____ The extraction scheme was clearly described, including all methodology.

10. ____ Sediment was analyzed at appropriate intervals.

11. ____ Sediments were adequately characterized.

12. ____ The appropriate degradates were analyzed for.

13. ____ Fish tissues (edible vs. viscera) were appropriately analyzed.

14. ____ Appropriate analytical methods were provided.

15.*____ Detection limits were reported.

16. ____ Pesticide concentrations in H_2O/fish were adequately reported.

17. ____ The test site (including soil type) was typical of the proposed use pattern.

18. ____ Specifics were provided regarding time of year, meteorological conditions during exposure, etc.

Criteria marked with a * are supplemental and may not be required for every study.

19. ____ A storage stability study was conducted using either spiked field or spiked laboratory samples to determine the stability of samples under typical lab storage conditions.

20. ____ Raw data in support of the Final Report are available.

Criteria marked with a * are supplemental and may not be required for every study.

165-5 Bioaccumulation in Aquatic Non-Target Organisms

GUIDANCE FOR SUMMARIZING STUDIES

Items in summary should include the items discussed in Chapter 2 of this package and the specific items listed below.

A. **Summary of Conclusions**

B. **Test Material**

1. The chemical structure
2. The purity of the test substance and pounds AI per acre applied
3. Solubility of the test material in water (include temperature and pH)
4. Reference additional studies that are presented to satisfy this data requirement and that are included in this summary package

C. **Description of the Requires Two Test Sites**

1. Identify the test location (including state, county etc) of each site
2. Description test soil and sediment type (USDA classification) and water characteristics (pH, hardness, sediment load, etc)
3. Description of soil and sediment characteristics
    a. % sand, silt, clay
    b. % organic material
    c. pH
    d. Cation exchange capacity (meq/100 grams)
4. Indicate other studies supporting this registration which use this soil and sediment
5. Description of environmental conditions during test
6. Description of pesticide use history of sites, if available
7. Topographical description of test sites

D. Test Methodology

1. Description of application method/rate and other field test data
2. Description of soil/sediment, fish and water sampling methodology and sampling intervals including pre-application, date of application and immediate post-application to maximum test duration (indicate hr, day, weeks)
3. Description of methods of analysis of soil/sediment, fish (whole body and edible tissue) and water samples including standards used and percent recovery
4. Description of sample storage conditions
5. Description of storage stability and results
6. Description of climatic conditions, including amount of rainfall or flood water, during test period
7. Description of flow data in terms of volume or linear flow

E. Reported Results

1. Description of residues in water and fish tissues (whole body and edible tissues) during the study period
2. Description of fish bioconcentration calculations and bioconcentration factors for fish uptake (whole body and edible) at each sampling period
3. Description of sample storage conditions prior to analysis
4. Description of sample storage stability study and results

F. Discussion of Results

SUBDIVISION O

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Relationship between Reregistration "Tracking Numbers" used in this package and Guideline Reference Numbers in the Subdivision O Pesticide Assessment Guidelines

	Phase 3 Tracking Number	Pesticide Assessment Guideline Number
Nature of the Residue - Plants	171-4(a)	171-4(a)(2)
Nature of the Residue - Livestock	171-4(b)	171-4(a)(3)
Residue Analytical Method	171-4(c)&(d)	171-4(b)
Magnitude of the Residue:		
Storage Stability	171-4(e)	171-4(c)(1)(ii)
Crop Field Trials	171-4(k)	171-4(c)(2)(i-iii)
Processed Food/Feed	171-4(l)	171-4(c)(2)(iv)
Meat/Milk/Poultry/Eggs	171-4(j)	171-4(c)(3)
Potable Water	171-4(f)	171-4(c)(4)
Fish	171-4(g)	171-4(c)(4)
Irrigated Crops	171-4(h)	171-4(c)(4)
Food Handling	171-4(i)	171-4(c)(5)

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171-3 Directions For Use

ACCEPTANCE CRITERIA

Special Instructions:

The following criteria are provided as guidance to registrants concerning the directions for use that should appear on product labels for food use chemicals. No summary for this guideline is required. Each registrant must have provided product labels to EPA; submission of these labels will satisfy the requirement to summarize 171-3.

Does your study meet the following acceptance criteria?

1. ___ Each formulation to be used identified with the concentration of active ingredient indicated (% by weight for solid formulations, pounds active ingredient per gallon for liquids)
2. ___ All crops which are to be treated with each formulation clearly identified
3. ___ Tolerance or exemption from tolerance proposed or established for each crop on label
4. ___ Impractical or unrealistic use restrictions excluded (eg., restricting feed use of corn forage not practical due to high economic value and common practice of feeding to livestock)
5. ___ Names and quantities of stickers, spreaders, or other adjuvants to be added to spray solution
6. ___ Field and orchard crop directions
   - ___ Application rate in quantity of formulation and pounds active ingredient per acre (For row or band treatments indicate if the rate refers to the area treated or to the entire field)
   - ___ Spray volumes to be used per acre
   - ___ Maximum number applications per year or growing season
   - ___ Minimum interval between successive applications
   - ___ Minimum interval between last application and harvest (preharvest interval=PHI)
   - ___ For orchard crops additional information for full coverage sprays (quantity of formulation and pounds active ingredient per 100 gallons spray) and concentrated sprays (amount active per acre should be related to tree size)
7. ___ Aerial, ultra low volume (ULV) and mist spray directions include spray concentration, amount of active ingredient per acre, and spray volume per acre
8. ___ Postharvest fumigation directions
   - ___ Dosage expressed in weight fumigant per volume of storage space or headspace or weight fumigant per unit weight of commodity treated
   - ___ Temperature, pressure and duration of exposure specified
   - ___ Geometry and airtightness of containers described
   - ___ Aeration procedures and time of aeration specified
   - ___ Minimum interval between successive applications

Criteria marked with a * are supplemental and may not be required for every study.

9. ____ Animal treatment directions
    - ____ Concentration of pesticide in treatment solution
    - ____ Quantity of spray, pour-on solution, dust, etc. to be applied per animal
    - ____ Amount of time animal to be held in dip tank
    - ____ Frequency of treatment
    - ____ Maximum number of treatments
    - ____ Preslaughter interval (interval between last treatment and slaughter) specified (interval longer than 3 days usually not considered practical)

10. ____ Aquatic use directions
    - ____ Dosage expressed in quantity of formulation and pounds active ingredient per surface acre or parts per million pesticide in the water (in latter case the amount product per surface area should be related to average pond depth)
    - ____ Detailed description provided for specialized equipment
    - ____ Minimum distance specified from treated area to potable water or irrigation intake pipe
    - ____ If oxygen depletion problems, proportion of pond to be treated and required interval between treatments
    - ____ Maximum number of applications per year
    - ____ Minimum interval between applications

11. ____ Food handling establishment use directions
    - ____ Type of establishment that may be treated
    - ____ Dilution instructions and spray concentration
    - ____ Type of application equipment and mode of application (space spray, directed spray to crevices, spot treatment, etc.)
    - ____ Dosage limitations including cubic and square foot limitations
    - ____ Frequency of treatment
    - ____ Time of treatment (eg., after-hours in restaurants)
    - ____ Instructions concerning removal and covering of food, dishes and utensils
    - ____ Cleanup procedures before food processing, preparation or serving resumes

12. ____ Agricultural premises treatments
    - ____ Description of areas to be treated (eg., feed lot, milking room, animal barn)
    - ____ Dosage specified (pounds per unit volume treated for fogging applications; concentration of active ingredient in spray solutions; weight active ingredient per unit area of feed lot)
    - ____ Frequency of treatment
    - ____ Directions as to whether animals should be removed during treatment

Criteria marked with a * are supplemental and may not be required for every study.

171-3 Directions For Use

GUIDANCE FOR SUMMARIZING STUDIES

Items in summary should include the items discussed in Chapter 2 of this package and the specific items listed below.

No summary for this guideline is required.

171-4(a) Nature Of The Residue -- Plants Study

ACCEPTANCE CRITERIA

Does your study meet the following acceptance criteria?

1. ____ Pesticide radiolabeled in non-labile portion of molecule (tritium label strongly discouraged)
2. ____ Specific activity sufficient to permit detection of low residue levels (0.01-0.1 ppm range)
3. ____ Radiochemically pure grade of active ingredient
4. ____ Pesticide applied to plant in manner simulating expected use
5. ____ Total radioactivity measured in plant parts used for human food or animal feed
6. ____ Extractability of residue into solvents determined
7. ____ Most of radioactivity extracted or exhaustive attempts (acid, base, enzyme) made to do so
8. ____ Major components or portion of the terminal residue identified (preferably by at least two techniques-e.g., TLC, HPLC, MS)

Criteria marked with a * are supplemental and may not be required for every study.

Subdivision O
Guideline Ref. No. 171-4(a)
December 24, 1989

171-4(a) Nature Of The Residue – Plants Study

GUIDANCE FOR SUMMARIZING STUDIES

Items in summary should include the items discussed in Chapter 2 of this package and the specific items listed below.

1. Chemical structure and name of test material with site of radiolabel indicated.

2. Specific activity of test material and detection limit achieved for treated commodities.

3. Radiochemical purity of test material.

4. Description of formulation and application of test material and comparison of application (rate, timing in terms of growth stage of crop) to expected use of pesticide.

5-7. Description of procedures used to quantitate and extract radioactivity. Summarize results in a table that includes for each crop part that has been analyzed the interval in days between the last application and collection of the sample, the total ppm radioactivity (usually in terms of ppm equivalents of parent pesticide), the % of the activity extracted into solvent(s), and, if acid, base or enzymatic hydrolyses were conducted, the % of additional total activity released by these procedures.

8. Description of procedures used to identify radiolabeled residues. Summarize results in a table that includes for each crop part that has been analyzed the interval in days between the last application and collection of the sample, the total ppm radioactivity, and the % of total radioactive residue (TRR) associated with each identifiable residue. Although the various identified residues may have been found in several different extracts or fractions of a crop part, the % given in the table should represent the % of the TRR in the entire crop part. Information on individual extracts or chromatographic fractions should be limited to the body of the report.

   If any information is available on the number and magnitude of components within the unidentified fractions, this should be included in the summary. For example, if an unidentified residue (32% of TRR) is known to consist of at least 5 discrete components, none of which is >10% of the TRR, indicate this somehow under this portion of the summary. Other useful information on the unidentified residue that should be presented in the summary, if known, include the proportions that are extractable (organic solvents, water), the proportions releasable by acid/base or enzymatic hydrolyses, and the partitioning behavior (organic solvents versus water).

9. Identification of the tolerance petition number, if the study has been used to support a tolerance.

Example:

1. Chemical structure and name of test material with site of radiolabel indicated.
N-methyl-3-bromoaniline; also known as "HERBICIDE"
The 14-C radiolabel was uniformly distributed through the phenyl ring.

2. Specific activity of test material and detection limit achieved for treated commodities.
Specific activity = 19.1 mCi/mg. The detection limits for treated soybean crop parts were 0.01-0.03 ppm.

3. Radiochemical purity of test material.
The radiochemical purity of ^{14}C-HERBICIDE was 98.5%.

4. Description of formulation and application of test material and comparison of application (rate, timing in terms of growth stage of crop) to expected use of pesticide.
Radiolabeled HERBICIDE was formulated as an emulsifiable concentrate by addition of the emulsifier and organic solvent used in the commercial product. The formulation was diluted with water and applied to the soybean foliage at the fourth-trifoliate stage at a rate equivalent to 0.25 pounds active ingredient per acre, twice the rate permitted on HERBICIDE labels. Soybeans would typically be in third to fourth-trifoliate stages when HERBICIDE is applied.

5-7. Description of procedures used to quantitate and extract radioactivity. Total radioactivities of all plant parts were determined by combustion of aliquots to $^{14}CO_2$. Samples were washed with hexane followed by blending and extraction with 20% methanol in acetone. In the case of dry crop parts, refluxing with 1N HCl was used to release additional residues. The total ppm found in plant parts and the distribution of the residues in the various solvents are summarized below.

Sample summary table - Total ppm in plant parts and the distribution of residues in solvents

Crop part	PHI	14-C total	% into hexane	% into acetone	% into 1N HCl	% not released
Green plant	2	27.5	75	20	--	5
Dry leaves	75	13.8	15	44	28	13
Dry stalks	75	2.9	10	50	23	17
Pods	75	0.7	3	35	40	22

PHI=preharvest interval in days; 14-C in ppm HERBICIDE equivalents

Extraction of the radioactivity in soybean seeds was not attempted due to the very low level of residue (<0.01 ppm).

8. Description of procedures used to identify radiolabeled residues.
Hexane washes and acetone extracts were analyzed directly by thin layer chromatography and autoradiography. R_f values were compared to authentic standards. The HCl solutions were extracted with ether and the latter examined by TLC also. The identities of spots were further confirmed by scraping the spots from the plates and examining them by mass spectrometry. The residues on each crop part are summarized in the following table in which "TRR" is total

radioactive residue, "4-hydroxy" refers to N-methyl-3-bromo-4-hydroxyaniline and "desmethyl" refers to 3-bromoaniline.

Sample summary table- Total radioactive residues for various crop parts

		% of TRR			
Crop part	Total 14-C	Parent	4-hydroxy	Desmethyl	Unidentd
Green plant	27.5 ppm	72%	12%	9%	7%
Dry leaves	13.8 ppm	24%	39%	11%	26%
Dry stalks	2.9 ppm	18%	42%	8%	32%
Pods	0.7 ppm	15%	27%	15%	43%

In all cases about half the unidentified residue was activity that could not be extracted by solvents or HCl. The remainder consisted of very polar materials based on their TLC behavior.

171-4(b) Nature Of The Residue – Livestock

ACCEPTANCE CRITERIA

Does your study meet the following acceptance criteria?

1. ____ Pesticide radiolabeled in non-labile portion of molecule (tritium label strongly discouraged)
2. ____ Specific activity sufficient to permit detection of low residue levels (0.01-0.1 ppm range)
3. ____ Radiochemically pure grade of active ingredient used for dosing
4. ____ Pesticide administered orally to animals for at least three consecutive days (or applied externally for at least 3 consecutive days using a method of application specified in label directions)
5. ____ Animals not preconditioned by dosing with unlabeled material
6. ____ Animals sacrificed within 24 hours of final dose or application
7. ____ Total radioactivity measured in edible tissues (muscle, fat, liver, ruminant kidney) and milk or eggs
8. ____ Extractability of residue into solvents determined
9. ____ Most of radioactivity extracted or exhaustive attempts (acid, base, enzyme) made to do so
10. ____ Major components or portion of the terminal residue identified (preferably by at least two techniques-e.g., TLC, HPLC, MS) in edible tissues and milk or eggs

Criteria marked with a * are supplemental and may not be required for every study.

171-4(b) Nature Of The Residue – Livestock

GUIDANCE FOR SUMMARIZING STUDIES

Items in summary should include the items discussed in Chapter 2 of this package and the specific items listed below.

1. Chemical structure and name of test material with site of radiolabel indicated.

2. Specific activity of test material and detection limit achieved for treated commodities.

3. Radiochemical purity of test material.

4. Description of animal diet and dosing procedure including ppm pesticide administered/ingested on total diet basis (dry weight) (or description of application procedure if dermal treatment involved).

5. Description of animal diet prior to dosing (if different than 4) and assurance that pesticide not included in feed.

6. Method of sacrifice and time in hours from final dose of radiolabeled material.

7-9. Brief description of procedures used to quantitate and extract radioactivity. Summarize results in a table that includes for each edible tissue and milk (or eggs) the total ppm radioactivity (usually in terms of ppm equivalents of parent pesticide), the % of the activity extracted into solvent(s), and, if acid, base or enzymatic hydrolyses were conducted, the % of additional total activity released by these procedures.

10. Description of procedures used to identify radiolabeled residues. Summarize results in a table that includes for each edible tissue and milk (or eggs) that has been analyzed the total ppm radioactivity and the % of total radioactive residue (TRR) associated with each identifiable residue. [Additional guidance on tables is provided in the related document "GUIDANCE FOR SUMMARIZING 'NATURE OF THE RESIDUE --PLANTS' STUDY".]

11. Identification of the tolerance petition number, if the study has been used to support a tolerance.

171-4(c) & (d) Residue Analytical Method

ACCEPTANCE CRITERIA

Does your study meet the following acceptance criteria?

1. ____ List of equipment, reagents and standards provided along with U.S. sources/suppliers of same
2. ____ Instrumentation and operating conditions described
3. ____ Detailed description of each step in procedure to enable use by competent analyst unfamiliar with method
4. ____ Discrete response for analyte
5. ____ Control values reasonably low compared to tolerance
6. ____ Adequate recoveries (generally ≥70%) obtained for fortifications at the tolerance level
7. ____ Recoveries don't vary significantly from sample to sample
8. ____ Evidence that aged residues extracted by procedure (may reference work in metabolism studies)
9. ____ Data showing that method releases and recovers bound residues (if latter of toxicological concern)
10. ____ Requirements for regulatory methods (as opposed to those used only for collecting residue data)
    - ____ Does not require untreated commodity as blank
    - ____ Does not require internal or procedural standard to correct for recoveries (Addition of internal standard in final step just prior to injection is acceptable for calibration of retention times. However, use of internal standard throughout entire procedure to correct for recoveries is not acceptable unless data are available on numerous samples of each matrix to show analyte and internal standard behave identically in each step.)
    - ____ Does not require exotic equipment or reagents
    - ____ Reasonably rapid in execution
    - ____ Specific to measure residue in presence of other reasonably expected pesticides
    - ____ Sensitive in relation to tolerance
    - ____ Confirmatory method available
    - ____ Method not claimed to be Confidential Business Information
    - ____ Does not use hazardous reagents (justification needed for use of benzene as solvent or diazomethane as methylating agent)

Criteria marked with a * are supplemental and may not be required for every study.

171-4(c) & (d) Residue Analytical Method

GUIDANCE FOR SUMMARIZING STUDIES

Items in summary should include the items discussed in Chapter 2 of this package and the specific items listed below.

1-3. Brief description of key steps and instrumentation used in analytical method.

4. Copies of representative chromatograms, spectra, etc. for reference standard, untreated samples, and treated or fortified samples illustrating response for analyte.

5-7. Summary table containing the control values and recoveries for tested commodities. (See Table I for sample summary table for analytical methods). It is preferable for the recovery column to list the individual values and the average recovery for each commodity. However, if a large number of samples have been examined, it would be satisfactory to list the range of recoveries along with the number of samples, the average recovery and the standard deviation. If more than one analyte was examined, additional columns may be added to the table or a separate table generated for each analyte.

8. Discussion/summary of data showing aged residues extracted by method.

9. Discussion/summary of data showing that bound or conjugated residues of toxicological concern are measured by method. If specific conjugates were added to samples and recoveries measured, the results could be included in the summary table for items 5-7.

10. For regulatory methods:
    - Statement that method does not require (1) untreated commodity as blank, (2) internal standards to correct for recoveries, and (3) exotic equipment or reagents.
    - Time (both work hours and total time) required to analyze a sample or set of samples.
    - Brief discussion of specificity of method including results of interference studies.
    - Detection limit of method, typical control values, and comparison of these to tolerances.
    - Brief description of confirmatory method.
    - Method not claimed to be Confidential Business Information.
    - Statement that method does not use hazardous reagents or justification for their use.

11. Identification of the tolerance petition number, if the study has been used to support a tolerance.

Table I. Sample summary table of analytical method

Sample	PPM Controls	PPM Fort.	% Recoveries	(Average)
Soybean forage (green)	<0.02-0.04	0.05	72, 78, 83, 95	(82)
		0.10	77, 80, 91, 94	(86)
		0.50	88, 96	(92)
Soybean vines (dry)	<0.02-0.05	0.20	68, 74, 80, 84	(77)
		0.50	71, 81, 87, 90	(82)
Soybeans	<0.02	0.02	65, 72, 75, 81	(73)
		0.05	75, 78, 91, 97	(85)
		0.10	85, 94	(90)
Peanuts	<0.01-0.02	0.02	70, 75, 80, 82	(77)
		0.05	76, 83, 87, 101	(87)
		0.20	83, 93, 95	(90)
Peanut hulls	<0.02	0.05	74, 83, 95	(84)
Peanut meal	<0.02	0.05	71, 87	(79)
Peanut oil	<0.02	0.05	87, 97	(92)

171-4(e) Storage Stability

ACCEPTANCE CRITERIA

Does your study meet the following acceptance criteria?

1. ____ Sample preparation and fortification described (or in cases where samples with weathered residues are used, history of crop and pesticide treatment provided)

2. ____ Storage conditions specified (temperature, containers, form of r.a.c., lighting, etc.)

3. ____ Dates of fortification (or harvest in case of field treated samples), placement into storage, sampling, and residue analysis provided

4. ____ All components of total toxic residue fortified into commodity (or present from field treatment with pesticide) and measured by validated analytical method(s) (description of latter provided or referenced)

Criteria marked with a * are supplemental and may not be required for every study.

171-4(e) Storage Stability

GUIDANCE FOR SUMMARIZING STUDIES

Items in summary should include the items discussed in Chapter 2 of this package and the specific items listed below.

1. Description of sample treatment prior to placement into storage. For field treated crops, description of mode, rate, and timing of pesticide application. For fortified samples, description of fortification procedure including form of sample (e.g., whole r.a.c., macerate, extract) spiked.

2. Description of form of sample and container placed into storage. Specification of storage temperature and lighting conditions.

3-4. Brief description of analytical method used to measure residues including validation/recovery data. Summarize in a **table** the residue levels found as a function of time for each commodity, analyte and fortification level combination. (See Table II for an example of such a table).

Table II. Residue levels

	Analyte	PPM	PPM after n months storage				
Commodity	spiked	spiked	0	1	3	6	12
Corn grain	Parent	1.00	0.97	0.86	0.89	0.91	0.82
" "	Metab1	0.50	etc........				
" "	Metab2	0.50	etc........				
Potatoes	Parent	0.50	etc........				
"	Metab1	0.20	etc........				
"	Metab2	0.20	etc........				

5. Identification of the tolerance petition number, if the study has been used to support a tolerance.

171-4(f) Magnitude of the Residue – Potable Water

ACCEPTANCE CRITERIA

Does your study meet the following acceptance criteria?

1. ____ Bodies of water treated according to label directions leading to maximum residues:
    - ____ Maximum application rate and number of applications
    - ____ Minimum retreatment intervals
2. ____ Data reflect modes of application on label: e.g., aerial, specialized equipment, treatment of pond margins only.
3. ____ Representative formulations examined
4. ____ Water sampled in center of treated area and at various points to show effect of distance on residue level
5. ____ Water sampled on day of treatment and later periods to show effect of time on residue level
6. ____ Sufficient number of trials conducted to determine an appropriate tolerance or maximum residue level (factors to consider include "geographic representation", seasonal and yearly variations, sizes and types of bodies of water treated, the toxicity of the pesticide)
7. ____ Total toxic residue measured in water by validated analytical method (description provided or referenced)
8. ____ Description of sample treatment, collection, handling and storage provided (covering periods from treatment to sampling and from sampling through residue analysis)
9. ____ Dates of treatment, sample collection, entry into storage, and residue analysis
10. ____ Storage stability data available reflecting storage of water samples (may be referenced to separate study)

Criteria marked with a * are supplemental and may not be required for every study.

171-4(f) Magnitude of the Residue – Potable Water

GUIDANCE FOR SUMMARIZING STUDIES

Items in summary should include the items discussed in Chapter 2 of this package and the specific items listed below.

1. Comparison of rate and number of applications and retreatment intervals to those permitted on product labels.

2. Comparison of application modes in study to those permitted on product labels.

3. Description of formulations tested and maximum residues found for each one.

4-5. Description of water sampling procedures with regard to distance from treated area, depth of samples, and time periods between application and sampling.

6. Discussion of how trials provide adequate estimate of the maximum residue level expected in water from actual use of the pesticide.

7. Brief description of analytical method used to measure residues including validation/recovery data. Summarize results of each trial in a table showing the effect of distance and time on residues.

8. Storage conditions for water samples between sample collection and residue analysis. [Sample treatment, collection and handling covered by items 1-5.]

9. Duration of storage of water samples between collection and residue analysis.

10. Summary of data showing stability of residues under storage conditions and duration similar to those described in items 8 and 9 (may be referenced to separate study).

11. Identification of the tolerance petition number, if the study has been used to support a tolerance.

171-4(g) Magnitude of the Residue – Fish

ACCEPTANCE CRITERIA

Does your study meet the following acceptance criteria?

1. ____ Fish maintained in water containing maximum pesticide residues permitted by product labels
2. ____ Fish sampled on day of treatment and later periods to show effect of time on residue level and the time required for residues to plateau
3. ____ Residue data obtained for bottom feeders (e.g., catfish) and predators (e.g., bass) in the case of fish and for molluscs (e.g., clams, oysters) and crustaceans (e.g., shrimp, crabs) in the case of shellfish
4. ____ Total toxic residue measured in fish by validated analytical method (description provided or referenced)
5. ____ Analyses reflect fish commodity definitions in the Pesticide Analytical Manual, Volume I
6. ____ If pesticide used in estuarine areas, data provided for whole fish protein concentrate and smoked, canned or other processed fish products
7. ____ Description of pesticidal treatment of water and collection, handling and storage of fish samples provided
8. ____ Dates of treatment, sample collection, entry into storage, and residue analysis
9. ____ Storage stability data available reflecting storage of fish samples between sample collection (i.e., sacrifice) and residue analysis (may be referenced to separate study)

Criteria marked with a * are supplemental and may not be required for every study.

171-4(g) Magnitude of the Residue – Fish

GUIDANCE FOR SUMMARIZING STUDIES

Items in summary should include the items discussed in Chapter 2 of this package and the specific items listed below.

1. Concentration of pesticide in water and comparison to maximum level permitted by product labels.
2. Time periods fish maintained in treated water prior to sampling for residue analysis.
3. Types of fish and/or shellfish analyzed for residues.
4. Brief description of analytical method used to measure residues including validation/recovery data. Summarize in a table the total toxic residue found for each type of fish or shellfish (including control or untreated samples) as a function of time kept in treated water.
5. Portion of fish/shellfish analyzed for residues.
6. Summary of data showing behavior of pesticide residues upon processing of fish.
7. Description of pesticidal treatment of water, procedure for collection of fish samples, and storage conditions of samples.
8. Duration of storage of fish samples between collection and residue analysis.
9. Summary of data showing stability of residues under storage conditions and duration similar to those in items 7 & 8 (may be referenced to separate study).
10. Identification of the tolerance petition number, if the study has been used to support a tolerance.

171-4(h) Magnitude of the Residue – Irrigated Crops

ACCEPTANCE CRITERIA

Does your study meet the following acceptance criteria?

1. ____ Crops irrigated with water containing maximum pesticide residues permitted by product labels
2. ____ Representative crops from each crop grouping in 40 CFR 180.34(f) examined for residues resulting from treated irrigation water
3. ____ Crops sampled for residues within one day of irrigation
4. ____ At least two field trials conducted for each representative crop
5. ____ Total toxic residue measured in crops by validated analytical method (description provided or referenced)
6. ____ Description of pesticidal treatment of irrigation water, irrigation technique, and collection, handling and storage of crop samples provided
7. ____ Dates of pesticidal treatment of water, irrigation of crops, harvest of crops, entry of crop samples into storage, and residue analysis
8. ____ Storage stability data available reflecting storage of crop samples (may be referenced to separate study)

Criteria marked with a * are supplemental and may not be required for every study.

171-4(h) Magnitude of the Residue – Irrigated Crops

GUIDANCE FOR SUMMARIZING STUDIES

Items in summary should include the items discussed in Chapter 2 of this package and the specific items listed below.

1. Concentration of pesticide in water at time of irrigation and comparison to maximum level permitted by product labels.

2. List of crops examined for residues resulting from treated irrigation water.

3. Time periods between irrigation and sampling of crops for residue analysis.

4. Number of trials conducted for each irrigated crop.

5. Brief description of analytical method used to measure residues including validation/recovery data. Summarize in a table the total toxic residue found for each irrigated crop (including control or untreated samples) harvested within 1-2 days after irrigation. Residues in samples collected after longer irrigation to harvest intervals, if available, should be included in the table with clear indication of the observed intervals.

6. Description of pesticidal treatment of water, irrigation techniques, and storage conditions of samples.

7. Time intervals between pesticidal treatment of water and irrigation and between harvest of crops and residue analysis.

8. Summary of data showing stability of residues in crops under storage conditions and duration similar to those described in items 6 and 7 (may be referenced to separate study).

9. Identification of the tolerance petition number, if the study has been used to support a tolerance.

171-4(i) Magnitude of the Residue – Food Handling

ACCEPTANCE CRITERIA

Does your study meet the following acceptance criteria?

1. ____ Pesticide applied in manner leading to highest residues in food that could result from actual use (factors to consider include spray concentration; type of spray [space, spot, crack and crevice]; interval between sprays if multiple applications permitted; food covered or uncovered)

2. ____ Foods representative of those to be present in treated facilities analyzed for pesticide residues (e.g., in case of cafeteria include meat, baked goods, oily food [butter, cheese], fresh fruits and vegetables)

3. ____ Foods sampled for residue analysis as soon as permitted after application and at various later times

4. ____ Pesticide residue measured in representative foods by validated analytical method (description provided or referenced)

5. ____ Description of sample treatment, collection, handling, and storage conditions/duration provided

6. ____ Storage stability data available reflecting storage of food samples from collection until residue analysis (may be referenced to separate study)

Criteria marked with a * are supplemental and may not be required for every study.

171-4(i) Magnitude of the Residue – Food Handling

GUIDANCE FOR SUMMARIZING STUDIES

Items in summary should include the items discussed in Chapter 2 of this package and the specific items listed below.

1. Description of establishment or room in which study conducted. Description of mode and rate of application and handling of food items (covered vs. uncovered; wrapping materials; temperature). Comparison of pesticide application and food handling to that specified on product labels.
2. List of foods placed in treated area and analyzed for pesticide residues.
3. Time periods elapsed between pesticide application and sampling of foods for residue analysis.
4. Brief description of analytical method used to measure residues including validation/recovery data. Residues observed in foods (covered and uncovered listed separately if both analyzed) should be summarized in a table showing the effect of time (from application to collection of samples) on residues.
5. Storage conditions and duration for food samples between sample collection and residue analysis. [Sample treatment, collection and handling covered by items 1 & 3.]
6. Summary of data showing stability of residues under storage conditions similar to those described in item 5 (may be referenced to separate study).
7. Identification of the tolerance petition number, if the study has been used to support a tolerance.

171-4(j) Meat, Milk, Poultry, Egg--Feeding

ACCEPTANCE CRITERIA

Does your study meet the following acceptance criteria?

1. ____ Compound(s) fed corresponds to residues expected on feed items
2. ____ Several dosages examined with one approximating intake expected from treated feed items, one or more representing exaggerated intake, and one control group
3. ____ Multiple animals included in each dosage group (preferably at least 3 for cattle and 10 for poultry)
4. ____ Duration of dosing adequate to ensure residues plateau in milk or eggs (preferably at least 4 weeks)
5. ____ Animals sacrificed within 24 hours of final dose
6. ____ Total toxic residue measured in edible tissues (muscle, fat, liver, cattle kidney) and milk or eggs of both control and treated animals using validated analytical method (description of latter given or referenced)
7. ____ Analytical method sufficiently sensitive (0.01-0.05 ppm)
8. ____ Description of handling and dosing of animals, feed consumption, and sample collection, handling and storage provided
9. ____ Storage stability data available reflecting storage of tissue, milk and egg samples prior to residue analysis (may be referenced to separate study)

Criteria marked with a * are supplemental and may not be required for every study.

171-4(j) Meat, Milk, Poultry, Egg--Feeding

GUIDANCE FOR SUMMARIZING STUDIES

Items in summary should include the items discussed in Chapter 2 of this package and the specific items listed below.

1. Compound(s) fed to animals and comparison to residues on feed items.

2. Dosages or feeding levels examined and comparison to expected dietary burdens with brief explanation of calculation of latter.

3. Number of animals in each dosage group or feeding level.

4. Duration of dosing and time at which residues were observed to plateau in milk or eggs.

5. Method of sacrifice and time in hours from final dose.

6-7. Brief description of analytical method used to measure residues including validation/recovery data and statement of detection limits for tissues, milk and/or eggs. Summarize the observed residues as a function of feeding level in tables. The milk/egg table should show the residues as a function of time so the point at which residues plateaued can be determined. For tissues, time is usually not a factor as sacrifice most often occurs within 24 hours of the final dose. However, if some animals are allowed a longer withdrawal period, these should be shown separately on the table. Unless one value is noticeably different than others in the same set, it would generally be adequate to provide the range of values observed for each tissue for each feeding level. Control values (i.e., samples from animals not ingesting the pesticide) should also be indicated. (See Tables III and IV for examples).

8. Brief description of dosing procedure, handling and diet of animals, average feed consumption (for each feeding level), and collection of tissue/milk/egg samples. [Storage addressed in item 9.]

9. Storage conditions and duration for tissues, milk and eggs between sample collection and residue analysis. Summary of data showing stability of residues under similar conditions (may be referenced to separate study).

10. Identification of the tolerance petition number, if the study has been used to support a tolerance.

Table III. Sample summary table for feeding studies -- Toxic residue in tissues

Feeding Level	Kidney	Liver	Muscle	Fat
	PPM Total Toxic Residue in Tissues			
0 ppm	<0.05	<0.05	<0.05	<0.05
5 ppm	0.15-0.37	<0.05	<0.05	<0.05
15 ppm	0.51-0.97	<0.05-0.09	<0.05	<0.05-0.12
50 ppm	1.37-1.93	0.24-0.33	<0.05	0.14-0.47

Table IV. Sample summary table for feeding studies -- Toxic residues in milk

PPM Total Toxic Residue in Milk

Day	5 ppm in diet	15 ppm in diet	50 ppm in diet
-1*	<0.01	<0.01	<0.01
1	<0.01	<0.01	0.03-0.07
3	<0.01	<0.01-0.04	0.21-0.37
7	<0.01	0.01-0.05	0.19-0.38
10	<0.01-0.02	0.02-0.08	0.25-0.43
14	≤0.01	0.03-0.07	0.21-0.35
28	≤0.01	0.02-0.08	0.28-0.41

*Day before dosing initiated (control samples).

171-4(j) Meat, Milk, Poultry, Egg–Dermal Treatment

ACCEPTANCE CRITERIA

These rejection criteria address studies in which the animals have been treated dermally with the pesticide (as opposed to oral ingestion).

Does your study meet the following acceptance criteria?

1. ___ Animals treated according to label directions leading to maximum residues:
    - †___ Maximum spray or dip concentration
    - †___ Maximum spray volume per animal or maximum time in dip tank
    - †___ Maximum quantity pour-on or dust formulation per animal
    - †___ Free access given to backrubbers and dust bags
    - ___ Minimum retreatment intervals
    - ___ Maximum number applications or data showing that milk or egg residues decline to non-detectable levels within the minimum retreatment interval specified on product labels

    †Registrant should write "NA" (not applicable) if this type of application is not registered.

2. ___ Each type of formulation and application technique tested (although dips and high pressure wetting sprays cover dusts and pour-ons, provided approximately the same amounts of active ingredient are applied per animal)

3. ___ Multiple animals included in each treatment group to show variation in residues (preferably at least 3 for cattle and 10 for poultry)

4. ___ Animals sacrificed within 1 to 3 days of final application

5. ___ Total toxic residue measured in edible tissues (muscle, fat, liver, cattle kidney) and milk or eggs of both control and treated animals using validated analytical method (description of latter given or referenced)

6. ___ Analytical method sufficiently sensitive (0.01-0.05 ppm)

7. ___ Milk or eggs collected and analyzed daily until residues plateaued

8. ___ Description of handling and pesticidal treatment of animals and sample collection, handling and storage provided

9. ___ Storage stability data available reflecting storage of tissue, milk and egg samples prior to residue analysis (may be referenced to separate study)

Criteria marked with a * are supplemental and may not be required for every study.

171-4(j) Meat, Milk, Poultry, Egg--Dermal Treatment

GUIDANCE FOR SUMMARIZING STUDIES

Items in summary should include the items discussed in Chapter 2 of this package and the specific items listed below.

1. Comparison of application rates, retreatment intervals, and number of applications in study to those permitted on product labels. If maximum number of applications not examined, data showing level of milk or egg residues after minimum retreatment interval has elapsed.

2. Formulations and application techniques tested.

3. Number of animals in each treatment group.

4. Method of sacrifice and time elapsed from final dose.

5-7. Brief description of analytical method used to measure residues including validation/recovery data and statement of detection limits for tissues, milk and/or eggs. Residues observed in edible tissues and milk or eggs. If different formulations and/or application techniques were examined, tabulate the results with a separate column for each formulation and/or application technique. The milk/egg table should show the residues as a function of time so the point at which residues plateaued can be determined. Also, if animals are sacrificed after various withdrawal periods, residues in tissues should be shown as a function of time. Unless one residue value is noticeably different than others in the same set, it would generally be adequate to provide the range of values observed for each tissue for each type of treatment. Control values (i.e., samples from animals not treated with the pesticide) should also be indicated.

8. Brief description of pesticidal treatment, handling and diet of animals, average feed consumption, and collection of tissue/milk/egg samples. [Storage addressed in item 9.]

9. Storage conditions and duration for tissues, milk and eggs between sample collection and residue analysis. Summary of data showing stability of residues under similar conditions (may be referenced to separate study).

10. Identification of the tolerance petition number, if the study has been used to support a tolerance.

171-4(k) Magnitude of the Residue – Crop Field Trials

ACCEPTANCE CRITERIA

Does your study meet the following acceptance criteria?

1. ____ Crop treated according to label directions leading to maximum residues:
    - ____ Maximum application rate and number of applications
    - ____ Minimum retreatment intervals
    - ____ Minimum preharvest interval
    - ____ Minimum spray volume

2. ____ Data reflects modes of application on label: ground, aerial, oil diluents, use of adjuvants such as surfactants and spreader/stickers

3. ____ Representative formulations examined

4. ____ Trial locations represent all principal growing regions (adequate "geographic representation") OR minor crop for which regional registration is accepted

5. ____ Sufficient number of trials conducted to determine an appropriate tolerance or maximum residue level (factors to consider include seasonal and yearly variations, differences in varieties and cultural practices, the importance of the crop, the toxicity of the pesticide and its ability to translocate, and the type of use-e.g., early season/pre-emergence versus late season foliar)

6. ____ Total toxic residue measured by validated analytical method (description provided or referenced) on all parts of crop used for food or feed (except for feed items which are restricted by product labels)

7. ____ Description of sample treatment, collection, handling (including any washing or trimming) and storage provided (covering periods from planting to harvest and from harvest through analysis)

8. ____ Dates of treatment, harvest, entry into storage, and residue analysis

9. ____ Storage stability data available reflecting storage of crop samples (may be referenced to separate study)

NOTE: Registrants should refer to the document "GUIDANCE FOR PHASE 2 OF REREGISTRATION FOR PESTICIDE MINOR USES AND LOW VOLUME PESTICIDES" to determine whether all of these data requirements apply to minor uses.

Criteria marked with a * are supplemental and may not be required for every study.

171-4(k) Magnitude of the Residue – Crop Field Trials

GUIDANCE FOR SUMMARIZING STUDIES

Items in summary should include the items discussed in Chapter 2 of this package and the specific items listed below.

1. Comparison of application rates, timings, and spray volumes in field trials to those permitted on product labels.

2. Comparison of application modes and spray additives in field trials to those permitted on product labels.

3. Formulations tested and maximum residues found for each one.

4-5. Brief discussion of how trials provide adequate "geographic representation" for the crop and sufficient data to determine the maximum residue level expected from actual use of the pesticide.

6-9. Brief description of analytical method used to measure residues including validation/recovery data (latter may be listed in a footnote to the summary table). Summarize the results of field trials for each crop in a table. At a minimum, the table should include information on location of each trial, the rate and number of applications, the type of application equipment (i.e., ground or aerial), the spray volumes (GPA=gallons per acre), the dates of applications (or intervals in days between applications), the time in days from the final application to harvest/sampling, and the level of the residue of concern.

If different portions of the residue are determined by separate analytical methods, the level of each portion should be listed along with the total residue. When more than one sample having the same location, rate and preharvest interval has been analyzed, the individual values should be shown rather than a mean. Residues on treated samples should not be corrected for controls. Correction for recoveries is not desirable, but if it has been done should be clearly indicated. Each crop part on which a tolerance is to be set (see Table II of Residue Chemistry Guidelines-Subdivision O) should be included within the table or a separate table may be generated for each crop part (e.g., corn forage, fodder, and grain). Any postharvest treatment of the samples such as washing or trimming should be noted. If different formulations or modes of application (e.g., pre-emergence versus post-E) result in significantly different residues, a separate table is advisable for each.

Application rates and timings other than the expected use should be included in the table to address issues such as the need for processing studies. However, registrants should use judgment in cases where a large proportion of the data is not representative of the proposed use. The usefulness of the summary table may be lost if extensive examination of it is necessary to determine which data are applicable to setting tolerances or estimating dietary exposure. As a related comment, data that obviously do not meet the rejection criteria should not be included in the table unless a written justification is provided.

Other information that needs to accompany this portion of the crop field trial summary includes residue values on untreated (control) samples and sample storage conditions and duration (and how the latter compare to controlled storage stability studies). As it may be difficult to put all this information plus that mentioned above in the table itself, it would be acceptable in most cases to provide the ranges of control values, storage periods, etc. from the field trials within the brief narrative summary preceding the table or as footnotes to the table. If trials are run in more than one year, the year should be indicated for each trial. When the field trials for one crop are located in more than one MRID# (or Accession #), the MRID# number for each trial should be shown within this section of the summary. A company study number, if assigned, would also be useful as it would allow more rapid location of the raw data when the latter need to be examined.

(See Table V for a case where all the studies fall under one MRID#).

10. Identification of the tolerance petition number, if the study has been used to support a tolerance.

Table V. Sample summary table for crop field trials -- Residue of parent pesticide plus metabolite on lettuce

Location	# & Rate of Appln	Equip & GPA	Dates of Appln	PHI	PPM Parent	PPM Metab	PPM Total
Town 1, CA	3 x 0.10	G 30	2/5, 2/19, 3/10	7	1.50	0.27	1.77
				14	0.82	0.47	1.29
Town 2, CA	3 x 0.08	A 8	3/8, 3/21, 4/7	15	0.52	0.21	0.73
Town, NY	2 x 0.10	G 25	5/2, 5/23	8	2.47	0.17	2.64
				4	1.34	0.35	1.69
Town, CO	3 x 0.10	G 35	6/9, 6/21, 7/3	4	0.28	0.30	0.58
Town, AZ	2 x 0.10	A 5	10/12, 10/28	13	0.37	0.08	0.45

Whole, unwashed lettuce heads were analyzed. Only obviously decomposed wrapper leaves were removed prior to analysis.

Application rate in pounds active ingredient per acre
G=ground application, A=aerial, GPA=gallons per acre
PHI= preharvest interval in days

Control samples contained <0.05-0.08 ppm apparent residues of parent and <0.05 ppm metabolite.
Lettuce samples from above trials were stored at -20°C for 2-6 months prior to residue analysis.
Storage stability studies using apples, wheat and lettuce showed no loss of residues after 12 months at -20°C (Reference, MRID#).
Recoveries from control lettuce samples spiked with 0.1 ppm parent and analyzed concurrently with the field treated samples were 78-103%. Recoveries of metabolite (0.05 ppm) were 72-97%. (If method has been submitted separately, provide MRID# or other appropriate reference.)

171-4(l) Processed Food/Feed

ACCEPTANCE CRITERIA

Does your study meet the following acceptance criteria?

1. ____ The raw agricultural commodity (r.a.c.) samples that were processed contained field-treated detectable residues (preferably at or above the tolerance) OR r.a.c. was treated in the field at exaggerated rates in an attempt to get detectable residues OR spiked r.a.c.'s were used with data available to show that r.a.c. residues exist solely on the surface

2. ____ The r.a.c. was processed using procedures simulating commercial practices

3. ____ The total toxic residue was measured with a validated analytical method (description provided or referenced) in the r.a.c. and all its byproducts listed in Table 2 of the Residue Chemistry Guidelines

4. ____ Description of pesticidal treatment and processing of r.a.c. and collection, handling and storage of samples provided

5. ____ Storage stability data available reflecting storage of r.a.c. and byproduct samples (may be referenced to separate study)

Criteria marked with a * are supplemental and may not be required for every study.

171-4(l) Processed Food/Feed

GUIDANCE FOR SUMMARIZING STUDIES

Items in summary should include the items discussed in Chapter 2 of this package and the specific items listed below.

1. PPM pesticide on raw agricultural commodity (r.a.c.). Description of procedure used to deposit pesticide residues on r.a.c. For field treated r.a.c.'s, description of mode, rate, and timing of pesticide application. For fortified samples, description of fortification procedure and summary of data showing r.a.c. residues exist solely on surface of crop.

2. Brief description of processing techniques with comparison to those employed commercially.

3. Brief description of analytical method used to measure residues including validation/recovery data. Levels of total toxic residue in the r.a.c. and by-products (including control samples) listed in Table II of Residue Chemistry Guidelines.

4. Storage conditions and duration for r.a.c. and byproducts between processing and residue analysis. [Description of pesticidal treatment and processing covered by items 1 & 2.]

5. Summary of data showing stability of residues under storage conditions described in item 4 (may be referenced to separate study).

6. Identification of the tolerance petition number, if the study has been used to support a tolerance.

171-5 Reduction of Residues

ACCEPTANCE CRITERIA

Does your study meet the following acceptance criteria?

A. DEGRADATION STUDIES

1. ___ Description of sample history provided for the raw agricultural commodity (r.a.c.). This could include items such as the pesticidal treatment (application rate, preharvest interval, where grown, etc.), date and location of purchase, and storage conditions from harvest or purchase until processing/washing/cooking

2. ___ Detailed description of residue reduction procedure used on r.a.c. Such procedures may include trimming, washing, peeling, cooking, or storage of the commodity under simulated commercial or home food preparation conditions.

3. ___ Description of handling and storage of samples from time of residue reduction procedure until analysis for residues

4. ___ Total toxic residue measured with a validated analytical method (description provided or referenced) in the r.a.c. both before and after the residue reduction procedure

5. ___ Storage stability data available reflecting storage of r.a.c. and "processed" samples from time of residue reduction procedure until analysis for residues

B. MONITORING STUDIES

1. ___ Description of sample history provided for the commodity being monitored. This could include items such as sampling location (state, city, supermarket - large chain or local store, etc.), brand (national vs.local), food form (e.g. frozen, canned or fresh peas), date and location of purchase, and storage and handling conditions from purchase until residue analysis

2. ___ Detailed description of the statistical design of the study. This should include discussions of representativeness of sampling (does the sampling provide adequate representation in terms of commodities, location, brands, types of processing, etc.), and accuracy and precision of results

3. ___ Total toxic residue measured with a validated analytical method (description provided or referenced) in the commodity

4. ___ Storage stability data available reflecting storage of samples from the time of sampling until residue analysis

Criteria marked with a * are supplemental and may not be required for every study.

171-5 Reduction of Residues

GUIDANCE FOR SUMMARIZING STUDIES

Items in summary should include the items discussed in Chapter 2 of this package and the specific items listed below.

A. DEGRADATION STUDIES

As noted on the previous page, the organization and content of the summary should follow the rejection criteria for the study.

1. Description of sample history for raw agricultural commodity.
2. Description of residue reduction procedure used on raw agricultural commodity.
3. Conditions and duration of storage of samples from time of residue reduction until analysis of residues.
4. Brief description of analytical method used to measure residues including validation/recovery data. Levels of total toxic residue in commodity both before and after residue reduction procedure.
5. Summary of data showing stability of residues in samples stored under similar conditions to those noted in item #3 (may be referenced to separate study).
6. Identification of the tolerance petition number, if the study has been used to support a tolerance.

B. MONITORING STUDIES

As noted on page 1, the organization and content of the summary should follow the rejection criteria for the study.

1. Description of sample history for monitored commodity.
2. Description of the statistical design of the study.
3. Brief description of analytical method used to measure residues including validation/recovery data.
4. Summary of data showing stability of residues in samples stored from purchase until residue analysis (may be referenced to separate study).
5. Identification of the tolerance petition number, if the study has been used to support a tolerance.

171-6 Proposed Tolerances

ACCEPTANCE CRITERIA

Does your study meet the following acceptance criteria?

1. ____ Tolerance expression includes complete, accepted chemical names of parent pesticide and metabolites of toxicological concern

2. ____ Tolerance includes proper name or description of commodity or crop group

3. ____ Tolerance high enough to cover any residue values reasonably expected based on residue data (i.e., tolerance not based on average residues, but on maximum residue)

4. ____ Tolerance not set higher than necessary unless inordinate multiplicity of tolerance levels needs to be avoided

5. ____ Specification of conditions of use of pesticide for food additive regulations covering use in food handling establishments

Criteria marked with a * are supplemental and may not be required for every study.

171-6 Proposed Tolerances

GUIDANCE FOR SUMMARIZING STUDIES

Items in summary should include the items discussed in Chapter 2 of this package and the specific items listed below.

No summary is required for this guideline requirement.

171-7 Reasonable Grounds in Support of Petition

ACCEPTANCE CRITERIA

Does your study meet the following acceptance criteria?

1. ____ Rationale of how residue data support tolerance
2. ____ Explanation of any aberrant residue values
3. ____ Explanation for omission or substitution of requirements set forth in Residue Chemistry Guidelines.
4. ____ Brief discussion on sensitivity of analytical method and its ability to measure total toxic residue

Criteria marked with a * are supplemental and may not be required for every study.

171-7 Reasonable Grounds in Support of Petition

GUIDANCE FOR SUMMARIZING STUDIES

Items in summary should include the items discussed in Chapter 2 of this package and the specific items listed below.

No summary is required for this guideline requirement.

171-13 Submittal of Analytical Reference Standards

ACCEPTANCE CRITERIA

Does your study meet the following acceptance criteria?

1. ____ 2 grams each of purified analytical standards provided for pesticide and principal degradation products or metabolites

2. ____ Reference standards sent to proper address:
Pesticide and Industrial Chemicals Repository (MD8)
U.S. Environmental Protection Agency
Research Triangle Park, North Carolina 27711

3. ____ Material Safety Data Sheet included as required by OSHA in 29 CFR 1910.1200

4. ____ Letter of transmittal accompanying standards
    - ____ Purity of standards
    - ____ Analytical methods used to assay standards
    - ____ Statement of principal impurities
    - ____ Purification procedures
    - ____ Storage requirements
    - ____ Special precautions for safe handling

Criteria marked with a * are supplemental and may not be required for every study.

171-13 Submittal of Analytical Reference Standards

GUIDANCE FOR SUMMARIZING STUDIES

Items in summary should include the items discussed in Chapter 2 of this package and the specific items listed below.

1. Description of sample submitted, including:
   - Name of pesticide and principal degradation products or metabolites
   - Purity
   - Analytical methodology used
   - Statement of principal impurities
   - Purification procedures
   - Storage requirements
   - Special procedures for safe handling

SUBDIVISION R

201-1 Spray Drift Droplet Size Spectrum 402
202-1 Spray Drift Field Evaluation 404

201-1 Spray Drift Droplet Size Spectrum

ACCEPTANCE CRITERIA

Does your study meet the following acceptance criteria?

1. ____ The test chemical used was either the proposed formulated end-use product or of the same formulation category as the end-use product to be registered.
2. ____ The percentage or degree of purity of the ai was reported.
3. ____ The application rate was reported.
4. ____ The physical properties of the in-tank formulation mix were given including surface tension, viscosity, density, vapor pressure, etc.
5. ____ The collection surfaces or devices were identified along with the equipment limitations (including the resolution of the microscopes, particle measuring systems, or air samplers, and the spread factor of the droplets on the various collection surfaces (cards) for droplet sizing).
6. ____ The test site was specified (e.g., wind tunnel or field evaluation).
7. ____ The environmental conditions that prevailed during the test (temperature, relative humidity, air velocity) were provided.
8. ____ The nozzles used were those most likely to be used and cause drift for the application of that pesticide or the intended use pattern.
9. ____ The nozzle pressure, flow rate, and orientation to the airstream were reported.
10. ____ The particle size distribution versus both cumulative percent volume and droplet number (frequency) were reported.

Criteria marked with a * are supplemental and may not be required for every study.

201-1 Spray Drift Droplet Size Spectrum

GUIDANCE FOR SUMMARIZING STUDIES

Items in summary should include the items discussed in Chapter 2 of this package and the specific items listed below.

A. Summary of Conclusions

B. Test Material

1. Test material used (formulation, etc.)
2. The purity of the test substance and pounds AI per acre applied
3. Physical properties of the in-tank formulation mix.

C. Test Methodology

1. Application rate/method

2. Full description of collecting surfaces/devices including limitations of such surfaces/devices

3. Identification and description of test site

4. Description of environmental conditions prevalent during testing (e.g. temperature, relative humidity, air velocity)

5. Nozzle type, size, pressure, flow rate and orientation to air stream and justification for use

D. Reported Results and Discussion

1. The particle size distribution versus cumulative percent volume (tabular format).

2. The particle size distribution versus droplet number (frequency distribution).

3. The results tabulated to indicate a 10, 50, and 90th percentile of particle size distribution with respect to droplet volume and number (tabular format).

202-1 Spray Drift Field Evaluation

ACCEPTANCE CRITERIA

Does your study meet the following acceptance criteria?

1. ____ The test chemical used was either the proposed formulated end-use product or of the same formulation category as the end-use product to be registered.
2. ____ The test site specified (e.g. open field, cropped field, forest, grove, etc).
3. ____ The environmental conditions which prevailed during the test [temperature at two levels, relative humidity, air velocity and direction, rainfall or watering regime (overhead irrigation systems)] were provided.
4. ____ A diagram of the plot or area was included in the report which indicates north, swath width, and orientation, prevailing wind direction, and location of the collections stations.
5. ____ The type of application equipment used was reported.
6. ____ The nozzles and associated equipment were those most likely to be used for the application of that pesticide or the intended use pattern.
7. ____ The estimated minimum and maximum nozzle-to-target height was reported.
8. ____ The application rate in quantity per unit area (of plant or land surface) or in quantity per minute flow rate (gallons-per-minute or liters-per-minute) was reported.
9. ____ Diluents or carriers as well as the extent of dilution were identified along with possible adjuvants, tank mixtures with other pesticides, and total spray volume.
10. ____ The physical properties of the in-tank formulation mix were given including surface tension, viscosity, density, and vapor pressure.
11. ____ Controls were used to note any possible decay or other loss of pesticide during the collection, transport, storage, and analysis.
12. ____ The distribution of the collection surfaces were of sufficient number to establish a definitive uninterrupted picture of deposits across the treated swath as well as outside the target area.
13. ____ The placement of the collection surfaces (either at the soil surface or at the height of the surrounding canopy) was reported.
14. ____ If air samplers were employed, were they at least three downwind locations (one at the farthest downwind site is preferable).
15. ____ The quantities of pesticide at each collection station were reported.
16. ____ The stability ratio (Barad is preferred) was calculated.

Criteria marked with a * are supplemental and may not be required for every study.

202-1 Spray Drift Field Evaluation

GUIDANCE FOR SUMMARIZING STUDIES

Items in summary should include the items discussed in Chapter 2 of this package and the specific items listed below.

A. Summary of Conclusions

B. Test Material

1. Test material used (formulation, etc.)
2. Percent AI in test material
3. Diluents, carriers, adjuvants contained in tank mixture
4. Physical properties of the in-tank formulation mixture (e.g. density, surface tension, viscosity, vapor pressure etc)

C. Test Methodology

1. Application rate/method
2. Full description of collecting surfaces/devices including limitations of such surfaces/devices and distribution of devices within the test site
3. Identification and description of test site (diagram).
4. Location of air samplers if used
5. Description of environmental conditions prevalent during testing (e.g. temperature, relative humidity, air velocity type, Barad stability ratio).
6. Nozzle type, size, pressure, flow rate and orientation to air stream, and justification for use
7. The speed, height, and type of the application equipment over the ground
8. The estimated nozzle-to-target height

D. **Reported Results**

1. The particle size distribution versus cumulative percent volume and versus droplet number (frequency) if the droplet size spectrum study was performed as part of the field evaluation (tabular format).
2. The calculated Barad stability ratio (tabular format).
3. The quantities of pesticide at each collection station and the intended quantity of pesticide per area (g/hectare) (tabular format).
4. The extent of downwind spray drift evaluated with respect to possible exposure to the non-target organism(s) that may be detrimentally effected (tabular format)

E. **Discussion of results**

1. Exposure assessment of spray drift to non-target organisms.

SUBDIVISION U

230-236 Applicator Exposure Monitoring: Passive Dosimetry 408

230-236 Applicator Exposure Monitoring: Passive Dosimetry

ACCEPTANCE CRITERIA

Does your study meet the following acceptance criteria?

1. ____ Typical end-use product of the active ingredient tested.
2. ____ End-use product handled and applied using recommended equipment, application rates, and typical work practices.
3. ____ Exposure monitoring using at least five replicates at each of at least three sites for each job function with the exception of pilots. Pilots should have at least three replications at each of at least three sites.
4. ____ Monitoring period is sufficent to collect measurable residues but not excessive so that residue loss occurs.
5. ____ Dermal and/or inhalation exposure monitored by validated methodologies. Biological monitoring is consistent with and supported by pharmacokinetic data accepted by the Agency.
6. ____ Quantity of active ingredient handled and duration of monitoring period reported for each replication.
7. ____ Clothing worn by each study participant and location of dosimeters reported.
8. ____ Quantitative level of detection is at least 1 $\mu g/cm^2$.
9. ____ Storage of samples consistent with storage stability data.
10. ____ Efficiency of extraction in laboratory provided as mean plus or minus one standard deviation. Lower 95% confidence limit is not less than 70% based on a minimum of seven replications per fortification level or prior Agency approval of extraction methodology provided.
11. ____ For each matrix at least one field fortification sample per monitoring period per fortification level. At least one field blank per worker per monitoring period for each matrix.
12. ____ When collecting urine for biological monitoring, collection should involve 24 hour urine samples. A minimum of one baseline, pre-exposure 24 hour sample must be collected. 24 hour samples must be collected for the day of application and for sufficient days postapplication as determined by the excretion profile of the pesticide.

Criteria marked with a * are supplemental and may not be required for every study.

230-236 Application Exposure Monitoring: Passive Dosimetry

GUIDANCE FOR SUMMARIZING STUDIES

Items in summary should include the items discussed in Chapter 2 of this package and the specific items listed below.

1. Form of pesticide tested.
2. Product handled and applied.
    a. equipment
    b. application rates
    c. total amount of material handled for each activity
    d. duration of monitoring periods
3. Pilots
    a. Number of sites monitored
    b. Number of replicates per site
4. Dermal and/or inhalation exposure and biological monitoring methods.
5. Clothing scenario studied for each study participant including location of dosimeters and comparison to label directions concerning clothing.
6. QA/QC data including quantitative level of detection, method efficiency, storage stability, field recovery for each matrix analyzed.
7. Number of field samples and blanks per worker per monitoring period.
8. Sample schedule for urine sample collection for biological monitoring.
9. Description of compound metabolism for biological monitoring.
10. Dermal and inhalation reported for each replicate and entire population as milligrams of exposure per pound of active ingredient handled (mg/lb/ai) and on a per hour basis; raw data should be reported as well as that corrected for field recovery (less than 100%).

APPENDIX D: OVERVIEW DOCUMENT FOR SUBDIVISION F

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OVERVIEW OF SUBDIVISION F

HAZARD EVALUATION: HUMAN AND DOMESTIC ANIMALS

This document provides an overview of the technical guidance for Subdivision F. Table D-1 lists EPA publications pertaining to Subdivision F that are available through the National Technical Information Service (NTIS). The first document on the list, the Pesticide Assessment Guidelines (PAG, sometimes referred to simply as "The Subdivision"), provides general guidance. It is supplemented by the Data Reporting Guidelines (DRG) published as a series of addenda. Table D-2 shows where to locate particular topics in the general guidance and Addenda. The body of the document reviews major changes since the guidance was originally published in 1982; clarifies some apparent inconsistencies between the Pesticide Assessment Guidelines, Data Reporting Guidelines, and Standard Evaluation Procedures; provides some new guidance; and indicates future directions that the Agency is considering.

The document is organized into parts to address the following categories of toxicity studies:

I. Acute Toxicity Studies
II. Subchronic Studies
III. Chronic and Long Term Studies
IV. Teratology Studies
V. Reproductive and Fertility Effects Studies
VI. Neurotoxicity Studies
VII. Mutagenicity Studies
VIII. Metabolism Studies
IX. Dermal Absorption Studies

Table D-1. EPA GUIDANCE DOCUMENTS FOR SUBDIVISION F

	NTIS Number	EPA Number
PESTICIDE ASSESSMENT GUIDELINES (PAG)		
Humans and Domestic Animals (revised)	PB86-108958	540/09-84-014
DATA REPORTING GUIDELINES (DRG)/ADDENDA		
Humans & Domestic Animals-Addendum 1	PB86-248184	540/09-86-150
Humans & Domestic Animals-Addendum 2	PB88-162292	540/09-88-023
Humans & Domestic Animals-Addendum 3	PB88-161179	540/09-88-024
Humans & Domestic Animals-Addendum 4	PB88-162227	540/09-88-028
Humans & Domestic Animals-Addendum 5	PB88-162219	540/09-88-029
Humans & Domestic Animals-Addendum 6	PB89-124077	540/09-89-007
Humans & Domestic Animals-Addendum 7	PB89-124085	540/09-89-008
Humans & Domestic Animals-Addendum 8	PB90-122227	540/09-90-071
STANDARD EVALUATION PROCEDURES (SEP)		
Guidance for Evaluation of Eye Irritation Testing	PB89-124572	540/09-88-105
Inhalation Toxicity Testing	PB89-100366	540/09-88-101
Oncogenicity Potential: Long Term Rodent Studies	PB86-129400	540/09-85-019
Teratology Studies	PB86-129392	540/09-85-018
Toxicity Potential: Subchronic and Chronic Exposure Studies	PB86-129418	540/09-85-020
OTHER GUIDANCE		
Position Document: Maximum Tolerated Dose	PB88-116736	540/09-88-003
Revised Policy for Acute Toxicity Testing	PB90-122151	540/09-90-072

Table D-2. WHERE TO FIND INFORMATION IN SUBDIVISION F GUIDANCE DOCUMENTS

TOPIC	LOCATION	
	Page in PAG	Addendum Number
I. Organization and Philosophy of Subdivision F	1	
II. The Standards for Acceptable Testing	3	
III. Discussion of Individual Tests	12	
80 OVERVIEW, DEFINITIONS, AND GENERAL REQUIREMENTS	20	
80-1 Overview	20	
80-2 Definitions	20	
80-3 General Provisions	21	
80-4 Reporting of Data	28	1-8
80-5 Combined Testing	32	
81 ACUTE TOXICITY AND IRRITATION STUDIES	34	
81-1 Acute Oral Toxicity Study	34	8
81-2 Acute Dermal Toxicity Study	39	8
81-3 Acute Inhalation Toxicity Study	44	6
81-4 Primary Eye Irritation Study	51	2
81-5 Primary Dermal Irritation Study	55	3
81-6 Dermal Sensitization Study	59	4
81-7 Acute Delayed Neurotoxicity of Organophosphorus Substances	62	5
82 SUBCHRONIC TESTING	66	
82-1 Subchronic Oral Toxicity (Rodent and Non-rodent):90-Day Study	66	8
82-2 Repeated Dose Dermal Toxicity: 21-Day Study	76	8
82-3 Subchronic Dermal Toxicity: 90-Day Study	83	8
82-4 Subchronic Inhalation Toxicity: 90-Day Study	92	6
82-5 Subchronic Neurotoxicity: 90-Day Study	103	5
83 CHRONIC AND LONG TERM STUDIES	107	
83-1 Chronic Toxicity Studies	107	8
83-2 Oncogenicity Study	117	8
83-3 Teratogenicity Study	126	1
83-4 Reproductive and Fertility Effects	130	8
83-5 Combined Chronic Toxicity/Oncogenicity Studies	137	8
84 MUTAGENICITY	147	
84-1 Purpose and General Recommendations for Mutagenicity Testing	147	8
84-2 Mutagenicity Tests	148	8
85 SPECIAL STUDIES	152	
85-1 Metabolism Study	152	7
85-2 Domestic Animal Safety Testing	156 (18)	
85-3 Dermal Absorption Studies of Pesticides (Reserved)	(19)	

I. ACUTE TOXICITY STUDIES

Guidelines 81-1, 81-2, 81-3 (for oral, dermal and inhalation toxicity) have been changed since 1982 to reflect the Agency's objective to reduce the number of animals used to evaluate acute toxicity while providing adequate information on chemical safety. A new Section (d) recommends the following:

1. use of existing data on structurally related chemicals
2. use of limit test
3. estimation of lethal dose
4. multiple endpoint evaluation

In 1984, Section (g) was changed to "A concurrent untreated control is not necessary. A vehicle control group should be run concurrently except when historical data are available to determine the acute toxicity of the vehicle." A proposal is under consideration to remove this requirement and not require any controls (as was the case in 1982).

The following changes refer to the "Revised Policy for Acute Toxicity Testing" issued on Sept. 22, 1988, and the proposed revisions to the acute oral, dermal and inhalation guidelines (in preparation) which are based on this revised policy. In the revised policy there were major changes under the headings "sex" and "numbers", as follows:

Sex: Where previous guidelines required equal numbers of animals of each sex for each dose level, the 1988 revised policy calls for consideration to be given to limiting studies to the more sensitive sex, using previous history on the chemical class to make the determination, and testing of a few animals of the other sex for confirmation.

Numbers: Where previous guidelines required at least 10 animals (5 of each sex) at each dose level, the 1988 revised policy urged the use of abbreviated test methodologies, whenever possible (approximate lethal dose, moving average method, up-and-down methods were suggested) which use the lowest feasible number of animals.

The 1984 revisions removed from one part of the guidance (Guideline 80-4) the requirement for measuring lethal dose within a 95% confidence interval of 20% of its median when technically feasible. Through an editorial oversight, the requirement was still referenced under (i) "Data and reporting" (3) "Test report". Under the 1989 proposal, this mistake will be corrected and the requirement will no longer appear in the revised guidelines.

II. SUBCHRONIC STUDIES

A. Subchronic oral toxicity (rodent and nonrodent): 90-day study (82-1).

The Agency has been informing registrants that one of the major purposes of the subchronic rodent study is to determine the proper doses for the chronic/oncogenicity study. We have also been informing them that all data relating to estimating the maximum tolerated dose and presenting results of dose-related effects should be presented in a clear manner.

Purpose

The 90-day oral subchronic toxicity study in the rodent may also be used to estimate the lowest dose level that is likely to induce life-threatening toxicity in the rodent chronic/oncogenicity feeding study. This dose level is referred to as the Maximum Tolerated Dose (MTD). When using the data obtained from the subchronic study for determining dose levels to be used for a chronic/oncogenicity feeding study, the MTD should be taken into account since it is desirable to determine the possible oncogenic effects induced by the test substance at as high a dose level as possible. It should be noted that estimation of the MTD from the subchronic study may require testing more than 3 dose levels. For further guidance on MTD's, a position paper on the selection of an MTD for oncogenicity studies (Pesticide Programs) has been published through NTIS, and additional information is provided in the Phase 3 Acceptance Criteria for Guideline Studies 83-2 and 83-5. It is recommended that a 90-day study be carried out on mice if a mouse oncogenicity study is planned.

Test procedures

When determining dose levels to be used for the rodent chronic/oncogenicity study, the MTD (the lowest dose level that is likely to induce life-threatening toxicity in a chronic/oncogenicity feeding study) should be estimated. Estimation of the MTD from the subchronic study may require testing more than 3 dose levels.

Data and reporting

- The histopathology data should be summarized in at least two ways:
    - A summary individual animal data table: for example, list individual animal number across the top of the table versus individual lesions by tissue (can be further broken down by grade within the table; i.e., P=present, 1=minimal, 2=slight, 3=moderate, A=autolysis, X=not remarkable, I=incomplete section, etc.) down the side of the table.
    - A summary lesion incidence table: for example, list dose group across the top of the table versus individual lesions by tissue down the side of the table. It is most important to include number of tissues examined per dose level in this table.
- When considering body weight changes, include body weight gains in treated animals when compared to controls (this is particularly helpful when estimating the MTD).
- Include food efficiency calculations (body weight gains versus food consumption). This is also useful when estimating the MTD.

B. Subchronic inhalation toxicity: 90-day study (82-4)

In specific cases the Agency has modified this requirement to a 21-day inhalation study. This requirement should be discussed with the Agency prior to proceeding with the study.

III. CHRONIC AND LONG TERM STUDIES

A. Chronic Toxicity Study (83-1)

The Agency has had problems interpreting data presented by registrants, especially histopathology data. Therefore we suggest the following:

- Histopathology data should be summarized in at least two ways:
    - A summary individual animal data table: for example, list individual animal number across the top of the table versus individual lesions by tissue (can be further broken down by grade within the table; i.e., P=present, 1=minimal, 2=slight, 3=moderate, A=autolysis, X=not remarkable, I=incomplete section, etc.) down the side of the table.
    - A summary lesion incidence table: for example, list dose group across the top of the table versus individual lesions by tissue down the side of the table. It is most important to include number of tissues examined per dose level in this table.
- When considering body weight changes, include body weight gains in treated animals when compared to controls.
- Include food efficiency calculations (body weight gains versus food consumption).

B. Oncogenicity study (83-2)

The following supplementary guidance is provided:

- Data should be available to indicate that the animals were tested at a sufficiently high dose level. For test chemicals of low toxicity, a limit dose of 1000 mg/kg body weight per day (dietary concentrations of approximately 20,000 ppm [2% in the diet] for rats or 7000 ppm [0.7% in the diet] for mice) is an adequate upper limit.
- The histopathology data should be summarized in at least two ways:
    - A summary individual animal data table: for example, list individual animal number across the top of the table versus individual lesions by tissue (can be further broken down by grade within the table; i.e., P=present, 1=minimal, 2=slight, 3=moderate, A=autolysis, X=not remarkable, I=incomplete section, etc.) down the side of the table.
    - A summary lesion incidence table: for example, list dose group across the top of the table versus individual lesions by tissue down the side of the table. It is most important to include number of tissues examined per dose level in this table. The table may also include separate tabulations and total tabulations for animals that either died or were sacrificed in moribund condition during the study and for animals that were sacrificed on a predetermined time schedule.
- When evaluating body weight changes, include body weight gains in treated animals when compared to controls.

- Include food efficiency calculations (body weight gains versus food consumption).

- When appropriate and feasible, historical control data should be provided for neoplastic lesions which were significantly increased in treated animals following administration of the test chemical and for particularly unusual nonneoplastic lesions which were identified in treated animals following administration of the test chemical. The historical control data should be presented by individual studies, tumor types, laboratories and sex (i.e. data presented as a range is not sufficient).

C. Combined chronic toxicity/oncogenicity studies (83-5)

The following supplemental guidance is provided:

- Data should be available to indicate that the animals were tested at a sufficiently high dose level. For test chemicals of low toxicity, a limit dose of 1000 mg/kg body weight per day (dietary concentrations of approximately 20,000 ppm [2% in the diet] for rats or 7000 ppm [0.7% in the diet] for mice) is an adequate upper limit.

- The histopathology data should be summarized in at least two ways:

    - A summary individual animal data table: for example, list individual animal number across the top of the table versus individual lesions by tissue (can be further broken down by grade within the table; i.e., P=present, 1=minimal, 2=slight, 3=moderate, A=autolysis, X=not remarkable, I=incomplete section, etc.) down the side of the table.

    - A summary lesion incidence table: for example, list dose group across the top of the table versus individual lesions by tissue down the side of the table. It is most important to include number of tissues examined per dose level in this table. The table may also include separate tabulations and total tabulations for animals that either died or were sacrificed in moribund condition during the study and for animals that were sacrificed on a predetermined time schedule.

- When evaluating body weight changes, include body weight gains in treated animals when compared to controls.

- Include food efficiency calculations (body weight gains versus food consumption).

- When appropriate and feasible, historical control data should be provided for neoplastic lesions which were significantly increased in treated animals following administration of the test chemical and for particularly unusual nonneoplastic lesions which were identified in treated animals following administration of the test chemical. The historical control data should be presented by individual studies, tumor types, laboratories and sex (i.e. data presented as a range is not sufficient).

IV. TERATOLOGY STUDIES

A. Clarifications

The discussion below clarifies Guideline Number 83-3 and indicates how EPA is applying the guidance. The letter and number designations follow those in the guidelines.

It should be recognized that this study is not a chronic or long term study and cannot be used as such for risk assessment purposes although listed under this heading in the Guidelines.

Teratology studies should more correctly be titled as "Developmental Toxicity Studies" as evaluation of other manifestations of developmental toxicity are required to be assessed in addition to malformations. This is also a necessary change in order to reflect that the submitted studies are consistent with the Agency's risk assessment guidelines.

(A) When Required. Postnatal studies are presently being required by the Agency on a case-by-case basis if it is deemed necessary to further evaluate any of the manifestations of developmental toxicity. There are plans to make this a conditional requirement.

(B) Purpose. This toxicity study is designed to determine the potential of the test substance to induce any of the manifestations of developmental toxicity in the fetus which may arise form exposure of the mother during pregnancy. The manifestations include (1) death (2) structural abnormality (3) altered growth and (4) functional deficiency. Functional deficiencies can generally be investigated only in postnatal studies.

(C) Definitions. As noted earlier, the Agency is concerned with more than just teratogenic effects and therefore, the definition for developmental toxicity needs to be provided.

(1) Developmental Toxicity - the study of adverse effects on the developing organism that may result from exposure prior to conception, during prenatal development, or postnatally to the time of sexual maturation. Adverse developmental effects may be detected at any point in the life span of the organism. The major manifestations of developmental toxicity include: (1) death of the developing organism, (2) structural abnormality, (3) altered growth, and (4) functional deficiency.

(D) Standard of the Test Method. In addition to the listed methodology, on a case-by-case basis the Agency may require a postnatal evaluation. This may necessitate additional groups of animals that are allowed to deliver normally with offspring evaluated to weaning or possibly to sexual maturity. Behavioral/developmental neurotoxicity batteries may be included as part of this assessment. See neurotoxicity discussed below.

(E) Substance to be Tested. Testing shall be performed in oral gavage studies with the technical grade of the active ingredient. In dermal exposure studies, testing is also preferred utilizing the technical grade but accompanying dermal absorption studies using both the technical grade and formulations that are marketed may also be required in order to allow for meaningful risk assessments to be performed. In addition, on a case-by-case basis, dermal developmental studies using the formulations marketed may be required if dermal irritation is deemed minimal (after consultation with the Agency). Only when no other alternative is available and only after the

Agency has been consulted, should dermal studies be conducted using an irritating formulated product.

(F) Limit Test. If an oral gavage dose level of at least 1000 mg/kg produces no evidence of developmental toxicity (even if some level of maternal toxicity is clearly present), studies at other dose levels may not be considered. There is no limit test for other routes of exposure.

(G) Test Procedures

(G)(1)(iv) Number. At least 20 pregnant rats, mice or hamsters or 12 pregnant rabbits are now required at each dose level and control group. Often 20 pregnant rabbits are necessary, especially in a repeat rabbit study designed to clarify the results of an initial study. The objective is to ensure that sufficient numbers of litters are available to permit meaningful evaluation of the potential developmental toxicity.

(G)(3)(ii) If a vehicle is used, its toxicological properties should be understood; it should not induce developmental or reproductive toxicity. Dermal studies should not be performed utilizing vehicles that are irritants unless all reasonable steps have been taken to reduce or eliminate potential irritation to the maternal animals and the Agency has been consulted prior to initiation.

(G)(3)(iii) To select the appropriate dose levels, a pilot or trial study is advisable using pregnant animals.

(G)(3)(iv) Although the Agency requires the highest dose level to induce some level of overt maternal toxicity such as weight loss, it is recognized that limiting maternal mortality to less than 10% may not always be possible. Such studies have routinely been accepted when mortality exceeds this level (but is less than 50%) and such severe effects (e.g. - mortality) do not extend into other dose levels. Studies where mortality may exceed 50% at the high dose level are considered on a case-by-case basis but dose related mortality must never reduce the numbers of litters available at the middle or low dose levels.

(G)(5) Administration of test substance. Oral gavage studies should be performed initially in order to ascertain the potential of a pesticide to induce developmental toxicity. If any studies are positive for developmental toxicity, and if worker exposure is anticipated, dermal developmental toxicity studies and dermal absorption studies should be carried out in order to allow the Agency to perform risk assessment. Before dermal studies are initiated concurrence from the Agency should be obtained.

(G)(7)(i,ii) Observation of animals. Careful clinical examinations for signs of toxicity should be made on a daily and not a weekly basis.

(G)(7)(v) Measurements of food consumption should be carried out in all developmental toxicity studies regardless of route of exposure.

(G)(7)(vi) Dams should be weighed at least every 2-3 days during gestation and at the time of sacrifice. In postnatal studies, pups should also be weighed at least at weekly intervals.

(G)(8)(i) Gross necropsy. At the time of sacrifice or death, dams should receive a thorough gross necropsy. If animals are found dead or moribund, a veterinary pathologist should specify the apparent cause of death/moribundity when possible.

(G)(8)(ii) Appropriate staining, glass plate techniques or other appropriate methodology should be employed to verify pregnancy and assist in accurate counts of early resorptions.

(G)(8) Better utilization and examination of (vi) mouse, rat, and hamster and (vii) rabbit fetuses involves dissection of the torso followed by clearing, staining and then skeletal examination of all fetuses. Half of the fetal heads are often dissected while the remainder are cleared, stained and receive a skeletal exam. Other acceptable methodology involves a series of sections of the heads followed by clearing, staining and skeletal examination. Care must be taken, however, (if these methods are to be accepted) to assure that a thorough examination of soft tissues of the head has been performed.

(H)(2) Evaluation of results. Historical data when necessary need to be provided for a period of two years prior to as well as two years after the date of the study to be submitted (when older studies are submitted). Data should be presented separately according to the route of administration. In addition, individual study data (dated) as well as means and ranges across studies need to be made available.

Studies must provide a NOAEL for developmental toxicity.

(H)(3) Test report. Although the litter is considered the most relevant unit for statistical assessment, data should also be presented and assessed on a fetal basis.

The test report must include all individual animal data as well as tabulated summary tables.

B. Future Planning

It has been recognized that the classical studies do not allow for assessment of all aspects of developmental toxicity. For example, almost nothing is learned relative to the potential for functional impairment from the cesarean derived litter. Hence, the Agency is more often requiring additional postnatal investigations. Sometimes these investigations help in further defining observed findings from the more classical cesarean studies or, in the case of developmental neurotoxicity testing, they may aid in further understanding central nervous system related developmental effects. Such Guidelines have been developed in the Agency and the triggers for requirement of these studies are currently being evaluated.

V. REPRODUCTIVE AND FERTILITY EFFECTS STUDIES

A. Clarifications

The discussion that follows clarifies Guideline Number 83-4 and indicates how EPA is applying the guidance. The letter and number designations follow those in the guidelines.

(E)(4)(II)(A&B) Test Procedures. (4)(ii)

After the conditions of (7)(i)B) are met, at the time of sacrifice, reproductive and target organs from all parental males in the dose groups and controls should be weighed and preserved for histopathological examination.

(E)(7)(iv)(A&B) Standardization of Litter Sizes.

Culling litters to 4 males and 4 females is not mandatory.

(E)(9)(i) Gross Necropsy.

Weights of the reproductive organs and identified target organs and pituitary (absolute and relative to body and to brain) should be provided.

A gross necropsy is required for:

1. All parental animals which are either scheduled sacrifice or are found dead or sacrificed moribund.
2. All pups found dead prior to day 21.
3. All weanlings not selected as parental animals of the next generation.
4. Not generally required for pups culled on day 4. However, should positive developmental effects be noted form other studies, necropsies should be considered.

Generally, if developmental toxicity studies have been conducted, findings from these studies need to be made available to the investigators of the reproduction study prior to the necropsies of offspring.

(E)(10) Clarification of Histopathology Requirements

Histopathology is required for:

1. Reproductive and target organs of all control and high dose P1 and F1 parental animals.
2. Organs showing pathology in the high dose level should then be examined in animals in the mid and low dose groups.
3. Although the Guidelines are not clear on required histopathology for animals that died or were sacrificed moribund, reproductive and target organs form these animals must be saved (unless autolysis prohibits) and receive histopathological examination. This has been standard policy for all toxicity studies.

4. Examination of day 21 offspring not selected as parental animals should also receive histopathological examination following the pattern required for parental animals. this is the only opportunity for examination of sexually immature offspring in the reproduction study.
5. Histopathological examination of pups culled on day 4 is not required.

B. Limit Test

The public has commented that there should be a "limit test" for reproduction studies (83-4). In response, it is suggested that the same limit test for chronic feeding studies be applied to reproduction studies, i.e. 1000 mg/Kg/day.

C. Evaluation of the Male Reproductive System

Over the last few years OPP has more and more routinely required additional testing relative to toxic effects of pesticides on the male reproductive system (other than what has been required by the 1982 Guidelines). Usually this has resulted from the generation of separate male studies (requiring the use of additional animals) since such data have rarely been available form existent reproduction studies. As a result, delays in some registrations and tolerances until these data are generated have been noted. These data are essential (during the risk assessment process) in allowing the Agency to assess the potential for sex specific differences in toxicity to pesticides and allowing it to regulate appropriately. In addition, when males from the reproduction study are utilized, no additional animals are utilized in order to obtain these data. Therefore, the following procedures should be incorporated as part of any newly generated reproduction studies in order to avoid prior difficulties:

1. Organ weights - (a) both testes should be weighted individually and identified as right or left, (b) epididymis - whole and cauda, (c) accessory sex glands (seminal vesicles with and without their fluid contents and prostate), and (d) pituitary.

2. Sperm - left testis (a) spermatid count, (b) total cauda epididymal sperm count (c) assessment of morphology and motility, and (d) epididymal fluid examined for debris and unexpected cell types. Video tape records are maintained as raw data allowing verification of reported results. Investigator methodology used for sperm motility assessment must be clearly presented in the submitted report.

3. Histopathology - the right testis is fixed in 10% neutral buffered formalin for at least 48 hours prior to embedding in glycol methacrylate, sectioning at 2 microns and staining with PAS hematoxylin. The right epididymis is fixed and retained for possible future examination.

D. Future Plans

OPP has considered the use of a modified version of the continuous breeding protocol to be allowed as an alternative to the 2-generation study specified in the Guidelines. As per policy established in a previous Agency workshop, reproduction studies must have two generations. Hence the Primary Continuous Breeding study modifications under consideration by the Agency deal with the addition of a second generation to the Continuous Breeding Study. Other considerations include the species to be tested (mouse or rat) and the advantages and disadvantages of using each as apparent from testing available to date.

At this point, the Office of Pesticide Programs is considering holding a workshop in order to further develop this protocol.

VI. NEUROTOXICITY STUDIES

A. Background

In a petition filed on February 12, 1987, the Center for Science in the Public Interest (CSPI) and a group of states, public interest groups, and professional societies sought to have EPA, under FIFRA, "issue testing methods necessary to fully assess the neurotoxic and neurobehavioral effects of pesticide active and inert ingredients and require that registrants undertake such tests for priority chemicals detailed herein".

They specifically proposed that EPA use the neurotoxicity guidelines developed by the Office of Toxic Substances (U.S. EPA, 1985,1988).

OPP convened a meeting of an expert subpanel of the FIFRA Scientific Advisory Panel on October 15-16, 1987 to review its proposed response to that petition (U.S. EPA, 1987). The Subpanel was requested to address a set of issues concerning when such testing might be appropriate to require for chemicals subject to FIFRA. In general, the SAP subpanel endorsed the use of:

- an observational battery, motor activity, and neuropathology as an acute and subchronic screening battery;
- further testing using tests of learned (operant) behavior, sensory testing, or other types of tests, or chronic testing, based on the results of the screening tests, and/or based on chemical class;
- developmental neurotoxicity testing under some circumstances based on chemical class, hormonal action, or data on adults.

The SAP Subpanel requested that the test guidelines for these data requirements be brought back to the SAP for review. OPP is revising its data requirements and testing guidelines for neurotoxicity testing. The SAP reviewed the new test guidelines on September 28, 1989. Among the revised guidelines is a new guideline for testing of Organophosphorus Substances for Delayed Neurotoxicity.

EPA is currently developing a Risk Assessment Guideline for Neurotoxicity for use throughout the Agency. This document will discuss general policy for the assessment of all types of neurotoxicity data, but will draw on the types of data in the test guidelines as illustrative of many types of neurotoxicity.

B. Planned Guideline Revisions

81-7 Acute Delayed Neurotoxity - hen
82-5 90 Day Delayed Neurotoxity - hen

OPP is planning to adopt a revised guideline for delayed neurotoxicity. This guideline will require range finding, acute, 4 day, and 20 day dosing regimens in hens in combination with assays of neurotoxic esterase (and acetylcholinesterase) to screen for this effect. It will provide more effective and convincing negative data sets than the previous requirement, facilitate interpretation of data, and improve the determination of NOELs for positive agents as well as an indication of whether further exposure would suggest an even lower NOEL.

The new guideline will replace Guidelines 81-7 and 82-5, Acute and Subchronic Delayed Neurotoxicity of Organophosphorus Substances.

81-x Acute neurotoxicity - rat

An acute neurotoxicity battery (Functional Observational Battery, Motor Activity, and Neuropathology) is proposed for the primary route of exposure, e.g. oral for food use, inhalation for fumigants, etc.. The battery may be associated with any one of the 3 acute toxicity studies, or, preferably, conducted as a separate study.

82-5 Subchronic neurotoxicity -rat

The subchronic neurotoxicity battery (same tests as the acute battery, listed above) is being proposed for the route of primary exposure for the use pattern and should generally be the same as the route for the acute study.

83-1 Chronic feeding - rodent

For new pesticides, if a chronic toxicity study in rats is needed, it should include a neurotoxicity battery (as described above). For old chemicals, adding a neurotoxicity battery to chronic studies will probably not be required.

Developmental Neurotoxicity -rat

A developmental neurotoxicity study in rats may be required for a variety of chemicals registered for different use patterns. It consists of exposure to dams through pregnancy and offspring through weaning. Testing will include the tests in the screening battery, as well as developmental landmarks, and tests of learning and memory. This end point will be evaluated in the postnatal developmental toxicity testing discussed above.

VII. MUTAGENICITY STUDIES

The only major deviation from the 1982 version of the Assessment Guidelines 84-1 and 84-2 is concerned with the adoption of specific protocol guidelines. The 1982 version suggests reference documents (e.g. Gene-Tox reports) for guidance on protocols. Although the Gene-Tox effort is supported by the USEPA, these documents are not official EPA policy. Protocol guidelines have been written by OTS and periodically undergo official revision and review (found in 40 CFR Part 798). OPP has informally adopted these protocol guidelines for the conduct of mutagenicity tests and this is a deviation which is regularly discussed with registrants. The upcoming Subdivision F revised guidelines which were reviewed by the SAP in September, 1989, will formally adopt these protocol guidelines as OPP policy. The adoption of these protocol guidelines alleviates some of the concerns and questions that have been brought up over the past few years. For example, i) it describes criteria for top dosing in tests, ii) statistical methods when appropriate is stated (many of the protocol guidelines state these are necessary, but for some studies, such as the Salmonella assay, there are no consensus statistical methods to use), iii) for the micronucleus test, the original "Schmid protocol" (2 doses, 24 hours apart with kill 6 hours after last dose) is no longer an acceptable protocol.

For the future, the mutagenicity section (Series 84) of the Subdivision F guideline will be revised. The revisions have been written and were reviewed by the OPP's SAP. There was also a public review period in association with the SAP review. The SAP met at the end of September, 1989. EPA is reviewing the SAP and public comments and the Agency will finalize the Subdivision F guideline for mutagenicity in the near future.

VIII. METABOLISM STUDIES

A metabolism study (85-1) may be performed and submitted in two parts:

1. Kinetics by individual dose
2. Metabolism by individual dose

IX. DERMAL ABSORPTION STUDIES OF PESTICIDES (RESERVED)

There is presently no guideline. The Agency is planning to produce a draft guideline (85-3) and supporting documents in 1990.

Registrants are advised to consult with the Agency **before** performing a dermal absorption study.

APPENDIX E: OVERVIEW DOCUMENT FOR SUBDIVISION O

OVERVIEW OF SUBDIVISION O:

RESIDUE CHEMISTRY GUIDELINES

This document provides an overview of the technical guidance for Subdivision O. Table E-1 lists EPA publications pertaining to Subdivision O that are available through the National Technical Information Service (NTIS). The first document on the list, the Pesticide Assessment Guidelines (PAG, sometimes referred to simply as "The Subdivision"), provides general guidance. It is supplemented by the Data Reporting Guidelines (DRG) published as a series of addenda. Table E-2 shows where to locate particular topics in the Pesticide Assessment Guidelines and Addenda. The body of the document reviews major changes since the guidance was originally published in 1982; clarifies some apparent inconsistencies between the Pesticide Assessment Guidelines, Data Reporting Guidelines, and Standard Evaluation Procedures; provides some new guidance; and indicates future directions that the Agency is considering.

There are three sections in this document. The first one is brief and contains general points that do not relate to any particular study. The second section addresses each residue chemistry study with (1) our responses to public comments on inconsistencies and (2) changes or clarifications that have been made in the guidelines since 1982. The third part of the document points out future changes being considered for a thorough revision and updating of the Guidelines.

Table E-1. EPA GUIDANCE DOCUMENTS FOR SUBDIVISION O

	NTIS Number	EPA Number
PESTICIDE ASSESSMENT GUIDELINES (PAG)		
Residue Chemistry, Subdivision O	PB83-153981	540/09-82-023
DATA REPORTING GUIDELINES (DRG)/ADDENDA		
Residue Chemistry-Addendum 1	PB86-203734	540/09-86-148
Residue Chemistry-Addendum 2	PB86-248192	540/09-86-151
Residue Chemistry-Addendum 3	PB87-208641	540/09-87-199
Residue Chemistry-Addendum 4	PB88-117270	540/09-88-004
Residue Chemistry-Addendum 5	PB88-124003	540/09-88-008
Residue Chemistry-Addendum 6	PB88-191713	540/09-88-049
Residue Chemistry-Addendum 7	PB89-124598	540/09-89-009
Residue Chemistry-Addendum 8	PB89-124606	540/09-89-010
STANDARD EVALUATION PROCEDURES (SEP)		
Analytical Methods/Residue Chemistry	PB90-103284	540-09-89-062
Directions for Use	PB88-243225	540/09-86-144
Magnitude of the Residue: Crop Field Trials	PB86-129426	540/09-85-021
Magnitude of the Residue: Processed Food/Feed Studies	PB88-243209	540/09-86-145
Qualitative Nature of Residue: Metabolism in Food Animals	PB90-103292	540/09-89-061
Qualitative Nature of Residue: Plant Metabolism	PB89-100333	540/09-88-102
Residues in Meat, Milk, Poultry and Eggs: Dermal Treatments	PB88-243217	540/09-88-092
Specialty Applications	PB88-244454	540/09-86-142
Storage Stability Study/Residue Chemistry	PB90-103276	540/09-89-063
OTHER GUIDANCE		
Position Document: Storage Stability	PB88-112362	540/09-88-002

Table E-2. WHERE TO FIND INFORMATION IN SUBDIVISION O GUIDANCE DOCUMENTS

TOPIC	LOCATION Page in PAG	 Addendum Number
170 SCOPE OF DATA REQUIREMENTS	1	
(a) General	1	
(b) Petitions for Tolerance	1	
(c) Minor Changes in Use Pattern	1	
(d) Food Use/Non-Food Use Determinations	1	
(e) Tobacco Uses	2	
(f) Aquatic Uses	2	
171-1 LIST OF REQUIREMENTS	2	
171-2 CHEMICAL IDENTITY	3	
(a) Active Ingredient	3	
(b) Inert Ingredient	4	
171-3 DIRECTIONS FOR USE	4	6
(a) Application Directions	4	
(1) Field and Orchard Crops	4	
(2) Animal Treatments	5	
(3) Fumigants	5	
(4) Aquatic Uses	6	
(5) Foreign Uses	6	
(6) Food Handling Establishments	7	
(7) Agricultural Premises	7	
(8) Miscellaneous Applications	8	
(b) Restrictions	8	
171-4 RESULTS OF TESTS ON THE AMOUNT OF RESIDUE REMAINING	9	2, 3, 4, 5, 7, 8
(a) Nature of the Residue	9	3
(1) Characterization of the Total Terminal Residue	10	3
(2) Nature of the Residue in Plants	11	3
(3) Nature of the Residue in Livestock	12	7
(b) Analytical Methods	13	2
(1) General Requirements	13	
(2) Validation of Method by Petitioner	14	
(3) Extraction Efficiency	14	
(4) Determination of the Total Toxic Residue	15	
(5) Requirements for Regulatory Methods	16	
(c) Magnitude of the Residue	17	
(1) General Considerations	17	
(i) Residues Determined	18	
(ii) Sampling	18	
(2) Design of Residue Experiments	19	
(i) Field Studies	19	2
(ii) Fumigation Uses	20	5

(iii) Slow Release Encapsulated Formulation Uses 20
(iv) Processed Food/Feed Studies 21 4
(3) Meat, Milk, Poultry and Egg Feeding Studies 22 8
(i) Residues in Feed Items 22
(ii) Direct Animal Treatment 24
(iii) Agricultural Premise Use Studies 24
(4) Potable Water, Fish and Irrigated Crop Studies 25
(5) Food Handling Establishment Uses 27

171-5 PRACTICAL METHODS FOR REMOVING RESIDUES THAT EXCEED THE TOLERANCE 30

171-6 PROPOSED TOLERANCES 30

171-7 REASONABLE GROUNDS IN SUPPORT OF THE PETITION 31

171-8 EXEMPTIONS FROM THE REQUIREMENT OF A TOLERANCE 31
(a) Active Ingredients 31
(b) Inert Ingredients 31

171-9 TOLERANCES FOR FOREIGN USE 32

171-10 ROTATIONAL CROP TOLERANCES 32

171-11 TOBACCO USES 33

171-12 FOOD USE/NON-FOOD USE DETERMINATION DATA REQUIREMENTS 34 5
(a) Seed Treatments 34 5
(b) Crops Grown for Seed Only 35 5
(c) Fallow Land 35
(d) Non-Bearing Crop Uses 35

171-13 SUBMITTAL OF ANALYTICAL REFERENCE STANDARDS 36

171-14 SPECIAL CONSIDERATIONS FOR TEMPORARY TOLERANCE PETITIONS 36

171-15 PRESENTATION OF RESIDUE DATA 37

171-16 TRANSLATION OF DATA 37
Table I. Categories and Representative Types of Food Establishments
Table II. RAC's, Processed Commodities, Feeds and Percents of Livestock Diets for all Crops

GENERAL POINTS

Typing errors and inadvertent omissions in the *text* portion of the 1982 Guidelines-Subdivision O are shown on Attachment 1 (Errata Sheet). Revisions that have been made to *TABLE II* of Subdivision O are shown on Attachment 2. The latter contains both inadvertent errors in the original published document as well as revisions such as the addition of new feed items, changes in the restrictability of livestock feed items, and lists of milled products for grains. [Note that guideline clarifications and changes in policy involving the *text* portion of Subdivision O are discussed below under "Individual Studies."]

Public comments on each type of residue chemistry study included "not enough guidance". EPA RESPONSE: Some areas will be discussed in more detail in a future thorough makeover of Subdivision O. At this time we emphasize that any future studies should be conducted in such a manner that all the acceptance criteria are met. These criteria are included elsewhere in the FIFRA '88 technical guidance package and represent the key features of an adequate study.

Another commenter noted that some DRG's have experimental results documented in the "Methods" section with the "Results" being a summary of these data. "Does EPA accept that a more logical approach is to keep *all* experimental data within the "Results" section, and to leave the summary to the "Conclusions" section?" EPA RESPONSE: Yes, we concur this is a more logical approach and would certainly have no objections to such a format. However, as long as reports are clearly written and contain the information noted in the DRG's, either of these formats is acceptable.

Registrants also commented on the location of figures and tables. "Does EPA accept that figures and tables are more easily accessible to readers when presented at relevant positions in the bulk of the report, rather than grouped together in a separate section at the end.....?" EPA RESPONSE: As long as tables and figures have accurate titles and are listed in the Table of Contents, either of these formats is acceptable.

INDIVIDUAL STUDIES

§171-4 Nature of the Residue-Plants

Comments

Commenters have provided a series of comments on this study to which we will respond below. We note that many of these comments are also applicable to the Nature of the Residue-Livestock study. The next four paragraphs deal with comments on how the nature of the residue study should be conducted.

COMMENT: The requirement to identify residues down to the 0.01 ppm level is "technically and scientifically unsound, difficult (or impossible) to achieve," and introduces new requirements. EPA RESPONSE: We agree that identification down to the 0.01 ppm level is difficult, but efforts to characterize such residues should be made. As noted in a recent Agency memo (ATTACHMENT 3), residue levels or trigger values have been proposed to the Agency by Ciba Geigy Corporation for the degree of characterization necessary for radiolabeled residues. These trigger values (0.01, 0.01-0.05, >0.05 ppm) are rough guides that registrants can use in their metabolism studies. However, as noted in our 7/25/89 memo, the degree of characterization should also depend upon how the application rate or dosage in the metabolism study compares to actual use of the pesticide. When low activity is found in crop parts or animal tissues following highly exaggerated application rates, characterization requirements should be less stringent.

COMMENT: With respect to the determination of total radioactivity in a plant part, it is difficult to obtain a representative subsample that will give accurate total 14-C by combustion for samples where the residue is not evenly distributed or which have a high water content. "For these types of samples, would it be acceptable instead to use a combination of extraction and combustion in order to determine the total residue? ... Since the weighed subsample is extracted by maceration, and the supernatant is separated by centrifugation, there are no losses due to 'work-up'. Radioactivity in the liquid extract is determined by LSC, and radioactivity in the solid residue (which will be much more evenly distributed than in the original sample) is determined by combustion and LSC."
EPA RESPONSE: Yes, we consider this procedure acceptable for the types of samples noted.

COMMENT: One registrant questioned why both polar and non-polar solvent systems should be used in thin layer chromatography of radioactive residues. "Should not the polarity of the solvent system be governed by the polarity of the compounds being analyzed?" EPA RESPONSE: Yes, the solvent polarity should be adjusted to the compounds of interest. We note that our copy of the SEP does not state "polar and non-polar solvent systems", but instead "at least two different solvent systems". Our main concern is that the residues be identified by matching Rf values in at least two different solvent systems if TLC is the only identification procedure being used. If possible, we really prefer that two separate techniques (e.g., TLC and MS) be used to identify residues (as opposed to TLC with two solvent systems).

COMMENT: Another comment questioned the need for frequent "interval sampling of protein, starch, lignin, and cellulose fractions.... Until a study is completed it is impossible to know whether bound residues of ≥10% are likely to occur." EPA RESPONSE: Only in those crop parts wherein ≥10% or ≥0.1 ppm of residue is bound does the registrant need to employ hydrolyses (acid, base, enzyme) in an attempt to release such activity. If this activity can not be identified as bound forms of the parent pesticide or closely related metabolites, attempts should then be made to show that the activity is associated with natural components such as starch or lignin.

The next five paragraphs address comments on the reporting of plant metabolism studies.

COMMENT: "The specific activity should be reported as μCi/mg instead of dpm/g or Curies/mole." EPA RESPONSE: Any units that would permit our calculation of ppm (mg/kg) radioactivity using reported counts (dpm, dpm/g, etc.) are acceptable.

COMMENT: "Reporting data as total radioactive counts is cumbersome, redundant, and unnecessary." EPA RESPONSE: Sufficient information on counts should be provided so that we can verify the ppm reported for crop parts, animal tissues, and the various chromatographic fractions thereof. If more convenient, another unit such as dpm/g may be used. Regardless of the unit used, a sample calculation should be submitted showing how the analyst arrived at "ppm" from the experimental data.

COMMENT: "Photographs of TLC plates should not be required. Chromatograms provide much more usable data." EPA RESPONSE: We agree "chromatograms" provide useful data and consider a TLC plate an example of one. Photos of TLC plates or their autoradiograms that were critical to the identification of residues should be provided. If HPLC coupled to a detector capable of measuring radioactivity was employed, then appropriate liquid chromatograms should be submitted. Regardless of the chromatographic technique used, chromatograms showing the behavior of the analytical standards should also be included in the report.

COMMENT: "The EPA asks that the total radioactivity in each plant part should be expressed as ppm equivalents of the total recovered plant radioactivity at the time of sampling or harvest. For many crops, e.g. apples, it would be extremely difficult to determine the "total plant radioactivity"......Does EPA require us to do this, or is it not more acceptable to express the residue in terms of Bq/ug, or ppm in crop parts of specific interest only? EPA RESPONSE: At a minimum registrants should report the total ppm radioactivity (usually in ppm equivalents of parent pesticide) for each crop part that could be used for food or feed. For those crops where the activity is measured in all plant parts, it would be useful to report the % of total plant activity in each part, but this is not required.

COMMENT: Enforcement methodology validation should not be reported in the nature of the residue studies, but rather in the magnitude of residue studies. EPA RESPONSE: We have no real preference on where the radiovalidation of analytical methods should be reported. It could be part of the report on the analytical method, part of the plant/animal metabolism study, or stand by itself as a report. The cover letter or summary of the full data package should indicate where it has been placed.

§171-4 Nature of the Residue-Livestock

Comments

Many of the comments discussed above on the Nature of the Residue-Plants study are also applicable to the livestock metabolism study.

Clarifications and Revisions

Registrants should note that the guidance on material to be fed in livestock metabolism studies is incorrect. The guidelines as published state that "The material fed should simulate the terminal residues in feed items as closely as possible...." This implies the studies should be carried out by dosing the animals with a mixture of radiolabeled chemicals. If animals are dosed with a mixture of parent and plant metabolites, one will be unable to determine whether plant metabolites are also animal metabolites. Therefore, the guidelines need to be revised to state that the animal metabolism studies should reflect feeding of one compound, usually the parent. If the plant metabolites are also found to be animal metabolites, then additional metabolism studies involving dosing with the plant metabolites will not generally be required. However, if a plant metabolite comprises a major portion of the residue on feed or is not found to be an animal metabolite, additional animal metabolism studies involving dosing with the plant metabolite may be required.

Additional clarification on when and how to conduct livestock metabolism studies was issued recently (ATTACHMENT 3). As noted in the SUMMARY at the end of that memorandum, livestock metabolism studies are now required whenever a pesticide is to be used on a crop having a livestock feed item in Table II of the Residue Chemistry Guidelines. (Registrants should refer to the original (1982) Table II as well as ATTACHMENT 2 to this Overview to determine if the crop of interest has a feed item.) This memorandum also provides "trigger values" (ppm radioactivity) for the degree of characterization needed in metabolism studies. These are applicable to both plant and animal metabolism studies and are also discussed earlier in this "Overview" under a comment on the Nature of the Residue-Plants study. Refer to ATTACHMENT 3 for more details.

§171-4 Analytical Methods

Comments

COMMENT: The statement that the enforcement method should "not require the use of an internal or procedural standard" is unacceptable. EPA RESPONSE: At this time we do accept the addition of an internal standard to the final extract just prior to injection to serve as a calibration for retention times. However, the use of an internal standard throughout the entire procedure to correct for recoveries is not acceptable unless data are available on numerous samples of each matrix to show analyte and internal standard behave identically in each step. [We are presently working with FDA and USDA to define what is a practical and acceptable enforcement method. This definition will become part of a future revision of Subdivision O. It is possible that the policy on internal standards will change as a result of this project.]

COMMENT: One commenter noted that a majority of their parent methods meet the requirement of a maximum of 24 hours for completion. However, many metabolite methods will not. "It is not in the interest of any company to develop methods which are more time consuming than necessary. This appears to be an 'inappropriate trigger' to be applied, and methods should be assessed on a case-by-case basis." EPA RESPONSE: The guidelines presently do include a case-by-case evaluation. "Methods taking longer than 24 hours will be considered acceptable on a case-by-case basis for minor metabolites or residues that are not acutely toxic." [This issue is also being examined in our work with FDA and USDA on defining a practical enforcement method.]

COMMENT: The SEP implies that "all matrices for which tolerances are proposed should be tested in the analytical method validation and recovery data etc. should be provided....Would it be possible to clarify that data for the appropriate typical crop types, e.g. root, leaf, oil and grain, would be sufficient?"

EPA RESPONSE: The analytical method should be validated on each crop for which residue data are generated and a tolerance is proposed. In the case of crop group tolerances, the method needs to be validated on only the representative crops for the group. With regard to where the validation data should be reported, we wish to point out that the report submitted on the method itself needs to include recovery data on only representative crops such as noted in the comment. However, in the crop field trial reports additional validation data should then be provided on any crop that was not tested for the analytical method report.

Clarifications and Revisions

The availability of an addendum to the Subdivision O Guidelines on multiresidue protocols was announced in the Federal Register in 1986 (Vol. 51, No. 187, 9/26/86, page 34249). Registrants are now required to test pesticides for their behavior through the multiresidue procedures used by FDA for monitoring residues [40 CFR 158.125(b)(15)]. The initial protocols were designated by Roman numerals (I-IV) and made available through the National Technical Information Service (NTIS) as Order No. 86 203734/AS. However, FDA recently published a revised version of these protocols as Transmittal 89-1 for the Pesticide Analytical Manual Volume I (PAM I). As part of this revision, Protocol II (the Storherr method) was removed as FDA no longer routinely uses this method. Also, a protocol was added to cover acids and phenols through PAM I 221.1. An updated version of the acid/phenol method in the Transmittal uses ion pair alkylation in place of diazomethane. In addition, to avoid confusing protocols and reporting forms with earlier versions, the protocols are now designated by letters (A,....E) instead of Roman numerals. Any future testing of pesticides for multiresidue behavior should use these new protocols.

> [Ordering information for Pesticide Analytical Manual. NTIS phone number 703-487-4600. Order Numbers are PB 889 117 99 for Volumes I + II; PB 889 118 99 for only Volume I; and PB 889 119 99 for only Volume II.]

Another requirement instituted since the 1982 publication of Subdivision O is the independent laboratory confirmation of tolerance enforcement methods. Pesticide manufacturers were informed of this requirement, which went into effect on 8/1/89, by PR Notice 88-5 issued 7/15/88. New tolerance enforcement methods must have been successfully tested by an independent laboratory prior to submission to the Agency. This requirement was initiated to ensure development of clearly written, complete descriptions of analytical methods.

Registrants should be aware that a strong justification is needed for the use of either diazomethane or benzene in an analytical method. A safer methylating agent or solvent, respectively, should be sought. If one can not be found, documentation should be provided supporting the need for use of these hazardous reagents.

§ 171-4 Storage Stability

Only limited discussion of this topic is present in the original Residue Chemistry Guidelines (page 19). However, it will become a separate line item in an upcoming revision of 40 CFR 158. In addition, the Agency published a Position Document on the "Effects of Storage (Storage Stability) on Validity of Pesticide Residue Data" in August 1987. This document, available through NTIS Order No. PB 88-112362, gives more details on the design and reporting of storage stability studies.

Comments

COMMENT: "Storage stability studies conducted on any member of a major crop group (root, leafy vegetable, cereal, oil) should be sufficient to satisfy the data requirement for each crop belonging to the group." EPA RESPONSE: As stated in the aforementioned Position Document, "Translating a storage stability study from one commodity to another will be considered appropriate only if both commodities are related (e.g., in the same crop group), and if the experimental design is considered appropriate to current considerations." The term "crop group" refers to the groups listed in 40 CFR 180.34(f). However, some combining of these groups into larger ones would generally be acceptable. Examples might be combining (1) leaves of root and tuber vegetables (group ii) with leafy vegetables (except Brassica) (group iv); (2) pome fruits (group xi) with stone fruits (xii); or (3) forage, fodder, and straw of cereal grains (group xvi) with grass forage, fodder and hay (group xvii).

COMMENT: "If storage stability has been shown in the raw agricultural commodity, storage stability studies in each of the processed fractions should not be required." EPA RESPONSE: Since some processed fractions (e.g., oils, fruit juices, soapstocks) have matrices quite different from the starting r.a.c., storage stability data are required for byproducts. However, once storage stability has been demonstrated in a few representative crops and their byproducts, additional data would not be needed, provided storage conditions and duration are similar. Suggested representative crops would be an oilseed (e.g., soybeans), a fruit (e.g., citrus), and a non-oily grain (e.g., wheat).

Clarifications and Revisions

For more details on storage stability requirements, registrants should refer to the aforementioned Position Document as well as the Data Reporting Guideline and Standard Evaluation Procedure.

§ 171-4 Crop Field Trials

Comments

COMMENT: Specific tables on geographic locations and recommended minimum samplings (size/weight/technique) should be included in Subdivision O. Such tables are included in the Guidelines for Conducting Agricultural Chemical Residue Field Trials in the USA. EPA RESPONSE: Such tables will probably be included in a future version of Subdivision O. With regard to locations for field trials, for the time being registrants may refer to ATTACHMENT 4 to this document. We remind petitioners that tolerances may be based on geographically limited residue data for minor uses as described in the 4/2/86 Federal Register notice (Volume 51, page 11341). With regard to sampling, registrants may refer to the Food and Agriculture Organization (FAO) Plant Protection Bulletin, Vol. 29, 1981, page 12 for their guidelines on pesticide residue trials. Our guidelines (page 19) state that the procedures described in this publication should be followed in the design and execution of field trials.

Clarifications and Revisions

Registrants should refer to ATTACHMENT 2 to this document for changes in the r.a.c.'s associated with certain crops. For example, feeding restrictions are no longer considered practical for sugar beet tops. Therefore, residue data on the latter must be included in requests for pesticide uses on sugar beets.

There are four areas which will receive more attention in reviews of future studies: plot size, random sampling, sample size, and sample reduction. Petitioners should be sure that in future field trials these four parameters are addressed in accordance with the aforementioned FAO Guidelines (pages 14, 17, 19, and 21, respectively) and described in sufficient detail in the field trial reports.

We reiterate that a policy addressing tolerances based on geographically limited residue data for minor uses was published in the Federal Register on 4/2/86 (Volume 51, page 11341).

§ 171-4 Processed Food/Feed

Comments

COMMENT: This section of the guidelines should include a table of concentration factors. EPA RESPONSE: In the future we plan to include theoretical maximum concentration factors in an updated version of Subdivision O.

COMMENT: "We are concerned about the requirement for storage stability data on individual processed fractions. For field corn, which may be processed into 25 or so different commodities, this represents an enormous and unnecessary waste of resources. It would be far better to get agreement that if the storage stability of the residues has been proven in the RAC, then this should cover all processing work." EPA RESPONSE: As noted earlier in this document in the section on Storage Stability, storage stability should be demonstrated in a few representative crops and their byproducts (e.g., soybeans, citrus, wheat). Once such stability has been shown, additional data would not be needed on processed fractions, provided storage conditions and duration are similar. With regard to field corn, we do not require data on 25 fractions. The processed commodities that need to be analyzed for grains are listed below.

Clarifications and Revisions

The original Table II stated that the processed commodities for grains included "milled products", but did not identify the latter by name. Since that time we have developed lists of these products and have added grain dust as a byproduct of corn, rice, soybeans, and small grains. These changes are included in ATTACHMENT 2 to this document. In addition, all the processed commodities are listed below for those crops which had the term "milled products" in Table II.

Crop	Processed Commodities
barley	hulls, bran, flour, pearl barley, grain dust
buckwheat	hulls, middlings, flour, grain dust
field corn	wet milling-starch, crude + refined oils dry milling-grits, meal, flour, crude + refined oils grain dust
guar	meal, gum
millet	hulls, flour, meal, grain dust
oats	hulls, flour, rolled oats, grain dust
rice	hulls, bran, polished rice, grain dust
rye	flour, rye feed (mix of bran, red dog flour, and middlings), grain dust
grain sorghum	flour, starch, grain dust
wheat	bran, flour, middlings, shorts, grain dust

If an adequate processing study has been conducted on wheat, it would satisfy the requirement for studies on barley, buckwheat, millet, oats, and rye. Guar, field corn, rice, and grain sorghum would each require their own processing study.

The grain dust data are needed only in those cases in which detectable, primarily surface residues are found on the grain. Early season herbicide uses usually result in low residues that would not be concentrated on the grain surface. Therefore, grain dust data would seldom be required in these cases. At the other extreme, postharvest treatments of stored grains virtually always trigger the need for grain dust data. Late season foliar uses to exposed grains such as wheat would also usually require such data.

Clarification regarding the need for processing studies when no detectable residues are present on the r.a.c. has been issued to EPA staff. The relevant portions of this guidance follow.

"If detectable residues are found on a crop for which Table II of the Guidelines lists a processed commodity, then a processing study is required, and if the data show a concentration of residues, then a Food Additive Tolerance (FAT) is required. The processing study should use RAC samples bearing detectable residues. However, if all RAC samples show no detectable residues as a result of the proposed use, then the reviewer may be able to make a conclusion as to the need for processing studies and FATs based on results of field trials carried out at exaggerated rates.

If exaggerated rate data are available and these result in detectable residues, then these samples should be used for a processing study. If residues concentrate on processing, then the concentration factor should be applied to the RAC tolerance level to arrive at the FAT level.

If exaggerated rate data are available and these result in no detectable residues, then no FAT is required provided that: 1) the rate was exaggerated by at least the theoretical concentration factor, 2) the data are sufficiently representative of important growing regions so that any reasonable potential for detectable residues has been realized, and 3) the exaggerated rate was not unrealistically high. This latter requirement arises over concern that if highly exaggerated rates are used the residue would not be distributed in the same proportion as if a 1X rate were used. For example, a 10X application of a granular formulation may result in a larger proportion of the pesticide falling to the ground. The level of exaggeration acceptable will depend on the use. For foliar application, a 5X exaggeration is likely to be an upper limit, but for other types of application, e.g., pre-emergent, a greater exaggeration may be acceptable.

If application of the highest practical exaggerated rate results in no detectable residues and the level of exaggeration is less than the theoretical concentration factor, then samples from this exaggerated rate can be the basis of a processing study. If no detectable residues are found in the processed product, then no FAT is required. If the processed commodity contains detectable residues, then a FAT is needed.

In cases where the RAC contains no detectable residues, the processing study will indicate only that the minimum concentration factor is the ratio of the concentration in the processed commodity to the limit of detection (LOD) in the RAC. The reviewer should evaluate all available data in determining the appropriate concentration factor. This will include, at a minimum, the metabolism studies and the chromatograms (or other raw analytical data) for the RAC samples. In some cases it may be possible to estimate residue levels from chromatograms where the response is below the limit of reliable quantitation but indicative of a "true" residue.

When using exaggerated rate data for consideration of FATs, reviewers should be careful not to set a FAT that is too high based on data not reflective of real-world use. Reviewers should also be careful not to require a FAT if there is no reasonable possibility that the processed product will bear residues higher than the RAC. Occasionally, use of exaggerated rate data will result in no clear indication of whether a FAT is needed, or, if it is needed, what level it should be. In these situations, considerable judgment, based on all pertinent data, will be required."

Registrants should use the above guidance for determining when processing studies are required and at what levels food or feed additive tolerances should be set.

§ 171-4 Meat, Milk, Poultry and Egg Feeding Studies

Comments

COMMENT: "There is no clear statement in the PAG that samples must not be composited (except for milk). The SEP states that samples must not be composited except in the case where small sample sizes are expected, e.g. eggs. ..... Three unique samples must be analyzed at every dose level. This is more than we are currently doing for poultry transfer studies."
EPA RESPONSE: Three unique samples of milk, eggs, and edible tissues should be analyzed at each dose level to show the variability of residues among different animals. In the case of cattle, this usually means one sample per animal as three cows are generally dosed at each level. For poultry, eggs or tissue samples from 3-4 birds may be composited to generate the three "unique" samples for each dosage group.

COMMENT: With regard to the SEP on dermal treatment of livestock, "To expect analysis of a formulation for impurities in the active ingredient is not responsible. Trace amounts of impurities will not be significant in these studies. .... The concentration of the impurities in the active ingredient in the formulation may therefore be calculated using the data in the confidential statement of formula for both the active ingredient and the formulation." EPA RESPONSE: The request for impurity information was intended to apply only to impurities which are actually regulated in the tolerance. Only a very small percentage of pesticides have such impurities. In those instances in which the impurity is regulated, the level of the impurity in the formulation applied to the animal should be measured to determine the actual exposure to that component. If the batch of technical grade active ingredient used to prepare the applied formulation was analyzed for the impurity of interest, the level of the impurity in the formulation could be calculated using the degree of dilution of the technical.

COMMENT: "The PAG states, 'Analysis must be conducted on whole milk and eggs (yolk and white)'. Does this mean analysis on yolk and white combined into one sample, or instead, separate analysis on each part?" EPA RESPONSE: The analysis should be conducted on the yolk and white combined into one sample. They may also be analyzed separately provided the weights of each are known so that the residue can be calculated on a whole egg basis.

Clarifications and Revisions

With regard to the possibility of waiving conventional livestock feeding studies when low residues are present in feed items, registrants should refer to ATTACHMENT 3. In some cases the livestock metabolism study may also serve as a feeding study and indicate that meat and milk tolerances are not necessary.

Registrants should refer to ATTACHMENT 2 for changes in the status of feed items. New feed items such as grain dust and potato waste have been added to the table. Sugar beet tops and wheat straw are examples of crop parts which can no longer be restricted as livestock feeds by label statements. In the case of corn, some %'s of the diet were discovered to be incorrect.

Registrants are reminded that the percents of the livestock diet in Table II of Subdivision O are on a dry weight basis. Therefore, for feeds with high moisture content such as fresh grass the residue level must be converted to a dry weight basis before utilizing the percent of the diet figures.

The text in the guidelines addressing the duration of feeding studies has been revised. The original guidelines state that "Generally, animals should be kept on test until residues plateau in milk or eggs. If no residues are detected in milk or eggs, animals should be kept on test for four weeks." These sentences should be replaced by: "Animals should be kept on feed for four weeks. However, if residues have not plateaued in milk or eggs by the end of four weeks, the feeding period should continue until a plateau is reached." This change was made to (1) address the possibility that the plateauing of residues in milk does not guarantee residues have plateaued in tissues and (2) to avoid situations wherein registrants terminate a study well before 28 days and the Agency does not agree a plateau was reached for milk or egg residues.

With respect to dermal treatment of livestock we generally do not consider preslaughter intervals (PSI) longer than 3 days as being practical. In dermal treatment studies the animals should be sacrificed within the PSI on the product label. However, as we have observed that residues may not peak in tissues until a week or so after application, additional data reflecting longer PSI's should be obtained to establish the maximum residue levels for tolerances.

§ 171-5 Reduction of Residues

In recent years there has been much interest on using residues in food as consumed ("anticipated residues") when conducting dietary risk assessments. Although there will be no further discussion of this topic in this "Overview", a chapter on "anticipated residues" is being prepared for inclusion in the FIFRA '88 Phase 3 Guidance Package. Registrants should refer to this chapter for additional information on market basket surveys and studies on degradation in storage, cooking, peeling, and washing. More detailed guidelines in this area are planned for issuance in mid-1990.

§171-12 Food Use/Non-Food Determination Data Requirements

One area in which numerous questions have arisen over the years is whether uses of pesticides on crops grown for seed are non-food uses, which do not require tolerances. Our concern has been that the crop may be diverted to food use before seeds are produced or that the seeds themselves may be used for food or feed, regardless of label statements prohibiting such practices.

The following two paragraphs outline the policy as published in the 1982 Guidelines. Please note that these paragraphs replaced the first paragraph published on page 35 in the original document (see ATTACHMENT 1-ERRATA SHEET).

"Uses on crops grown for seed only are considered to be non-food uses if (1) subsequent to treatment the crop is not fit for consumption by humans and is not fed to livestock, and (2) there is no likelihood of residues in crops grown from the harvested seed. Otherwise, such uses are considered to be food uses requiring tolerances.

Examples of uses where the crop is considered unfit for consumption subsequent to treatment are post-bloom applications to leafy vegetables and Brassica (cole) leafy vegetables, and desiccant uses on okra and root and tuber vegetables. These uses would qualify as non-food uses provided there is no likelihood of residues in crops grown from the harvested seeds. Factors affecting this include the level of residues on the harvested seed, the half-life of seed residues, the weight of the seed in relation to that of the subsequent crop, and the amount of residue uptake into the aerial portion of the crop."

In recent years we have accepted some uses which do not meet requirement (1) noted above. If a state is willing to provide assurance that seed crops will not be diverted to food or feed and information on acreage and cultural practices is provided, we will consider pesticidal treatment of crops grown for seed as a non-food use under 24(c) registrations. The information on cultural practices should emphasize those practices which distinguish the seed crop from the corresponding food crop and which would render the seed crops commercially unviable for food. Examples of such practices might be smaller crop spacing preventing adequate root formation and planting in a different season to encourage bolting versus head formation.

Once the State's assurance and cultural practice information outlining a rationale as to why these are non-food uses have been submitted, we will consider these uses on a case-by-case basis for 24(c) registrations. Most cole crops, leafy vegetables, and root crops have a good chance of obtaining pesticidal treatment of their seed crops on a non-food basis. Crops where the seeds themselves are major raw agricultural commodities such as grains, beans, and peas have very little chance of such registrations on a non-food basis. Alfalfa, clover and grass grown for seed are generally not considered non-food uses since they can be cut for hay prior to going to seed and the seeds or seed screenings may end up in livestock feed. However, we have recently accepted use on alfalfa grown for seed in Washington State based on rules issued by the State governing the use of the seeds, seed screenings and other crop parts.

NOTE: FOR THE FOLLOWING RESIDUE CHEMISTRY GUIDELINE NUMBERS, NO SPECIFIC COMMENTS WERE RECEIVED AND WE HAVE NO REVISIONS OR CLARIFICATIONS.

§ 171-4	Magnitude of the Residue-Potable Water
§ 171-4	Magnitude of the Residue-Fish
§ 171-4	Magnitude of the Residue-Irrigated Crops
§ 171-4	Magnitude of the Residue-Food Handling
§ 171-6	Proposed Tolerances
§ 171-7	Reasonable Grounds in Support of Petition
§ 171-8	Exemptions from the Requirement of a Tolerance
§ 171-9	Tolerances for Foreign Uses
§ 171-10	Rotational Crop Tolerances
§ 171-11	Tobacco (See ATTACHMENT 1-ERRATA SHEET re page 34)
§ 171-13	Submittal of Analytical Reference Standards
§ 171-14	Special Considerations for Temporary Tolerance Petitions
§ 171-15	Presentation of Residue Data
§ 171-16	Translation of Data

FUTURE REVISIONS OF RESIDUE CHEMISTRY GUIDELINES

This section of the "Overview" points out changes that are being considered for an updating of Subdivision O in the next few years.

With regard to ruminant metabolism studies, significant differences have been observed between goats and cows in the amounts of metabolites from some pesticides. Since cattle contribute much more to the human diet, future ruminant metabolism studies may be limited to cows only. In addition, swine metabolism studies may be required in the future whenever a feed item for swine is treated with a pesticide. Presently, these studies are required only when metabolism in ruminants differs from that in non-ruminants. Future livestock metabolism studies may also have to include identification of residues in feces and urine.

We are working with FDA and USDA to define what is a practical and acceptable enforcement method. As noted previously in this "Overview", issues to be addressed include the length of time needed for analyses and the use of internal standards.

Several projects are being conducted to update Table II. Food processors have been surveyed to determine the quantities of byproducts and their uses in animal feed. Experts in animal nutrition will be consulted to determine the percentages of assorted feeds in livestock diets. The gathered information will be used to update the processed commodities and feed items in Table II along with the %'s in the diet. The practicality of feeding restrictions for crops such as small grain forages, the vines and hays of peas/beans/peanuts, and sorghum forage and fodder will be investigated. We also plan to change some of the names for raw agricultural commodities to eliminate confusion over what is to be analyzed. For example, the terms forage and fodder have different meanings depending on profession and/or location. Words such as "green vegetative growth stage" may be used in the future. Theoretical concentration factors for some processed commodities will also be in the new table.

Radiolabeled studies may be required to determine what degradates are formed by pesticide residues upon cooking, canning, frying and other high temperature processes. The latter occasionally result in significantly higher levels of toxic residues with the best known examples being daminozide to UDMH and the EBDC fungicides to ETU.

Future livestock feeding studies may need to include an additional dosage level below the so-called "1x" level, which represents tolerance residues on all feed items. The additional dose will be used to more accurately predict "anticipated" or average residues in animal products. Although meat/milk tolerances would still be based on the 1x level, dietary risk assessments would usually use the results of a lower feeding level.

ATTACHMENT 1-"ERRATA SHEET"
ATTACHMENT 2-"REVISIONS IN TABLE II"
ATTACHMENT 3-"Guidance on When and How to Conduct Livestock Metabolism Studies"
ATTACHMENT 4-"SUGGESTED STATES FOR CROP FIELD TRIALS"

ATTACHMENT 1

Pesticide Assessment Guidelines
Subdivision O
Residue Chemistry

ERRATA SHEET

This Attachment lists the typing errors that were made in the text portion of the original guidelines in 1982. Note that typing errors were also made in Table II of the original Subdivision O. These are included in Attachment 2 to this "Overview" of the Residue Chemistry Guidelines along with other changes made in Table II since 1982 (e.g., sugar beet tops may not be restricted as a feed item; potato waste is now considered to be a feed item). Guideline clarifications and changes in policy that involve the text portion of Subdivision O are discussed in the body of the "Overview" under the appropriate study (e.g., what material to feed in livestock metabolism studies; when are processing studies needed).

Page 4 Second to last paragraph, last line
Change: "other use relevant use limitations"
To: "other relevant use limitations"

Page 7 Second paragraph, first line
Change: "For domestic pesticides uses"
To: "For domestic pesticide uses"

Page 8 Second paragraph, line four
Change: "in which pesticide are applied"
To: "in which pesticides are applied"

Third paragraph, first line
Change: "Clearly written and practical uses"
To: "Clearly written and practical use"

Page 18 Second paragraph, line 15
Change: "samples of these crop should"
To: "samples of these crops should"

Page 19 Third paragraph, line four
Change: "Vol. 24"
To: "Vol. 29"

Page 21 Last two lines
Delete all words following "data indicate that"

Page 23 Third paragraph, last line
Change: "part (b)"
To: "part (ii)"

Page 24 Last paragraph, first line
Change: "When the use of pesticides in agricultural buildings are such"
To: "When the use of pesticides in agricultural buildings is such"

Page 30 Third paragraph, line 8
Change: "it may be appropriate to propose combined tolerance for"
To: "it may be appropriate to propose a combined tolerance for"

Page 32 First paragraph, lines 12 and 13
Change: "toxicologically-innocuous, then additional data will be required. In some case"
To: "toxicologically innocuous, then additional data will be required. In some cases"

Page 34 Paragraph (2)
Change: "(2) Pyrolysis products derived from the active ingredient must be characterized."
To: "(2) Total residues on cured or dried tobacco. If residues at 0.1 ppm or more are detected, the determinations in the next paragraph are required.
(3) Pyrolysis products derived from the active ingredient must be characterized and the level of residue in smoke must be quantified."

Page 35 First paragraph
Replace the first paragraph with the following 2 paragraphs.

"Uses on crops grown for seed only are considered to be non-food uses if (1) subsequent to treatment the crop is not fit for consumption by humans and is not fed to livestock, and (2) there is no likelihood of residues in crops grown from the harvested seed. Otherwise, such uses are considered to be food uses requiring tolerances.

"Examples of uses where the crop is considered unfit for consumption subsequent to treatment are post-bloom applications to leafy vegetables and Brassica (cole) leafy vegetables, and desiccant uses on okra and root and tuber vegetables. These uses would qualify as non-food uses provided there is no likelihood of residues in crops grown from the harvested seeds. Factors affecting this include the level of residues on the harvested seed, the half-life of seed residues, the weight of the seed in relation to that of the subsequent crop, and the amount of residue uptake into the aerial portion of the crop."

ATTACHMENT 2

Pesticide Assessment Guidelines
Subdivision O
Residue Chemistry

REVISIONS IN TABLE II

This Attachment lists the revisions that have been made in Table II of the Residue Chemistry Guidelines since 1982. This list includes both typing errors from the original document as well as changes such as new feed items (e.g., potato waste) and elimination of practical feeding restrictions (e.g., sugar beet tops). Typing errors in the *text* portion of the original Subdivision O are shown in ATTACHMENT 1 to this "Overview". Guideline clarifications and changes in policy that involve the text portion of Subdivision O are discussed in the body of the "Overview" under the appropriate study.

Addition of Grain Dust

Since this revision affects numerous crops, it will be listed here for emphasis and convenience. "Grain dust" should be added under "PROCESSED COMMODITIES" and "FEEDS" for the following crops: barley (page 41), buckwheat (page 42), corn, field (page 44), millet (page 49), oats (page 50), rice (page 53), rye (page 53), sorghum, grain (page 54), soybeans (page 54) and wheat (page 57). With regard to the %'s of the livestock diets, the figure "20" should be placed under all types of animals in Table II. Data on grain dust from wheat will cover barley, buckwheat, millet, oats, and rye. The other crops will each need their own study. Also, as described on page 9 of the Overview, grain dust data are needed only when detectable, primarily surface residues are present on the grain. [This requirement was instituted due to the increased usage of grain dust in animal feed as a result of laws restricting its disposal.]

Page 40

Alfalfa

Change "Forage(G)(2)" to "Forage(G)(3)" and "NU(3)" to "NU(2)". [These footnotes were inadvertently reversed in the original published guidelines.]

Page 41

Barley

Delete "Hay" from the "RAC" and "FEEDS" columns and all its corresponding numbers across the chart. Delete "Germ" and "Milling products" in the "PROCESSED COMMODITIES" column and replace with the terms "Hulls, Bran, Flour, Pearl Barley". Also, add "Grain dust" as specified above. ["Hay" was deleted since it is not a significant feed item. "Milling products" were defined to clarify which commodities need to be analyzed.]

Beet, garden

Change "Greens" to "Leaves" in the "RAC" column. [The term was changed to clarify the part of the plant that makes up the RAC.]

Page 42

Buckwheat

Delete "Bran" and "Milled products" in the "PROCESSED COMMODITIES" column and replace with the terms "Hulls, Middlings, Flour". Also, add "Grain dust" as specified on page 1 of this

ATTACHMENT. ["Milled products" were defined to clarify which commodities need to be analyzed.]

Page 43

Chicory

Add the term "Roots" under the "RAC" column. ["Roots" was inadvertently omitted from the published document.]

Citrus

Delete "Peel" under "PROCESSED COMMODITIES". [Citrus peel is not a significant food or feed item.]

Page 44

Corn, field

Delete all the terms under "PROCESSED COMMODITIES" and replace with the following:

"Wet Milling
  Starch
  Crude oil
  Refined oil
 Dry Milling
  Grits
  Meal
  Flour
  Crude oil
  Refined oil"

Also, add "Grain dust" as specified on page 1 of this ATTACHMENT. In the row "Silage" under the columns "BEEF" and "DAIRY", change the numbers "25 10" to "30 50". ["Milled products" were defined to clarify which commodities need to be analyzed. Several percent of the diet figures in the published guidelines were incorrect.]

Corn, pop

In the row "Fodder(G)" under the columns "BEEF" and "DAIRY", change the numbers "30 50" to "25 10". [These figures were incorrect in the published guidelines.]

Corn, sweet

Delete the "(G)" following "Forage" in the "FEEDS" column. In the row "Cannery waste" under the columns "BEEF" and "DAIRY", change the numbers "30 50" to "25 10". [With the possible exception of uses limited to Florida, we do not consider a feeding restriction on sweet corn forage to be practical. The percent of the diet figures in the published guidelines were incorrect.]

Page 45

Dates

Under the column "PROCESSED COMMODITIES" add the term "Dried". [This commodity was inadvertently omitted from the published guidelines.]

Page 46

Flax

Delete "Hulls" from both the "PROCESSED COMMODITIES" and "FEEDS" columns and all its corresponding numbers across the chart. [Flax hulls are no longer considered a significant feed item.]

Page 47

Guar

Delete "Milled products" and replace with "Meal" and "Gum". ["Milled products" were defined to clarify which commodities need to be analyzed.]

Page 48

Lentils

Add "(G)" after both "Forage" and "Hay" in the "FEEDS" column. [We have concluded that a feeding restriction for these commodities is practical.]

Page 49

Millet

Delete "Milled products" under "PROCESSED COMMODITIES" and replace with "Hulls, Flour, Meal". Also, add "Grain dust" as specified on page 1 of this ATTACHMENT. ["Milled products" were defined to clarify which commodities need to be analyzed.]

Mint

Add "(G)" after "Spent hay" in the "FEEDS" column. [We have concluded that a feeding restriction for this commodity is practical.]

Mustard

Delete "Seeds" from the "PROCESSED COMMODITIES" column and add it to the "RAC" column. [Since mustard seed is harvested in the field, it is a raw agricultural commodity and not a processed commodity.]

Page 50

Oats

Delete "Hay" and "Hulls" under the "RAC" column. Also delete "Hay(G)" under "FEEDS" and its corresponding numbers across the chart. Under "PROCESSED COMMODITIES" delete "Milled products" and replace with "Hulls, Flour, Rolled Oats". Also, add "Grain dust" as specified on page 1 of this ATTACHMENT. [Oat hay is not a significant feed item. "Milled products" were defined to clarify which commodities need to be analyzed.]

Page 51

Peppermint

Add "(G)" after "Spent hay" in the "FEEDS" column. [We have concluded that a feeding restriction for this commodity is practical.]

Page 52

Potato

Delete "Dried" under "PROCESSED COMMODITIES" and add "Wet peel" and "Dry peel". Add "Processed potato waste" under "FEEDS" and the following percents of livestock diet: BEEF-50, DAIRY-25, TURKEY BROILERS-NU, LAYING HENS-10, SOWS/BOARS-50, FINISHING SWINE-50. Feed additive tolerances for processed potato waste should be based on the maximum concentration factor observed for residues in/on granules, wet peel, or dry peel. [Potato waste has been determined to be a significant livestock feed item.]

Page 53

Rape

Under "PROCESSED COMMODITIES" replace "Oil" with "Crude oil" and "Refined oil". [This makes the requirements for rape seed oil consistent with those of other vegetable oils.]

Rice

Delete "Milled products" under "PROCESSED COMMODITIES" and replace with "Bran". Under "FEEDS" delete the "(G)" after "Straw". Also, add "Grain dust" as specified on page 1 of this ATTACHMENT. [It has been determined that a feeding restriction for rice straw is not practical. "Milled products" were defined to clarify which commodities need to be analyzed.]

Rye

Delete "Milled products" under "PROCESSED COMMODITIES" and replace with "Flour, Rye feed (mix of bran, red dog flour, and middlings)". Also, add "Grain dust" as specified on page 1 of this ATTACHMENT. ["Milled products" were defined to clarify which commodities need to be analyzed.]

Safflower

Under "PROCESSED COMMODITIES" replace "Oil" with "Crude oil" and "Refined oil". [This makes the requirements for safflower oil consistent with those of other vegetable oils.]

Page 54

Sorghum, grain

Replace "Milled pdts" with "Starch" under "PROCESSED COMMODITIES". Also, add "Grain dust" as specified on page 1 of this ATTACHMENT. [This is to clarify which commodities need to be analyzed.]

Soybeans

Under "RAC" and "FEEDS" delete "Straw" and its corresponding numbers across the chart. Also, add "Grain dust" as specified on page 1 of this ATTACHMENT. [Soybean straw is not a significant feed item.]

Spearmint

Add "(G)" after "Spent hay" under the "FEEDS" column. [It has been determined that a feeding restriction is practical for this commodity.]

Page 55

Sugar beet

Delete the "(G)" after "Leaves" under "FEEDS". [A feeding restriction for sugar beet leaves or tops has been determined to be not practical.]

Add the following three crops after "Sunflower" on page 55:

CROP	RAC
"Sweet potato (yam)	Root
Swiss chard	Fresh
Taro	Root Foliage"

[These crops were omitted in the published guidelines.]

Page 56

Tomato

Under "PROCESSED COMMODITIES" replace "Puree" and "Catsup" with "Puree or Catsup". [Data on one product suffices for the other due to similar water content.]

Page 57
Wheat

Under "RAC" delete "Hay" and under "FEEDS" delete "Hay(G)" and all its corresponding numbers across the chart. Delete "Milled products" under "PROCESSED COMMODITIES" and replace with "Bran, Flour, Middlings, Shorts". Delete the "(G)" after "Straw" under the "FEEDS" column. Also, add "Grain dust" as specified on page 1 of this ATTACHMENT. [Wheat hay is not a significant feed item. "Milled products" were defined to clarify which commodities need to be analyzed. Since wheat straw is a major by-product and is fed in times when roughage is in short supply, the grower restriction for wheat is not appropriate.]

Footnote (3)

Revise to "G-Under grower control and not routinely fed to livestock; therefore, subject to label restrictions against feeding." [This revision clarifies that there are two factors to consider in the practicality of feeding restrictions. First, the feed item needs to be in control of the grower (i.e., does not leave the farm). Second, the feed item can not be of such importance that it will be routinely fed regardless of label restrictions. For example, alfalfa hay is a valuable animal feed and is virtually always raised for that purpose. Therefore, a label statement prohibiting feed use of alfalfa hay would often be ignored.]

ATTACHMENT 3

July 25, 1989

MEMORANDUM

SUBJECT: **Guidance on When and How to Conduct Livestock Metabolism Studies.**

FROM: Richard D. Schmitt, PhD, Chief
Dietary Exposure Branch
Health Effects Division (H7509C)

TO: Dietary Exposure Branch Staff

This memo is intended to clarify when livestock metabolism studies are needed and the efforts that should be made to identify residues in such studies. The emphasis will be on those cases where low or non-detectable residues are observed in feed items. The need for conventional livestock feeding studies in such situations will also be addressed.

For many years Branch policy called for livestock metabolism studies only when detectable residues of concern were found in feed items in crop field trials. This procedure discriminates against registrants who develop more sensitive methods for measuring residues in crops. In recent times we have requested animal metabolism studies in some instances when no detectable residues are present in feed items. However, this procedure has not been consistently applied. Effective with this memorandum, it will be Branch policy to require livestock (ruminant and/or poultry) metabolism studies whenever a pesticide is to be applied to a crop having an animal feed listed in Table II of the Residue Chemistry Guidelines. In addition to not discouraging the development of more sensitive methods for crop residues, this policy will provide some information on the potential transfer of residues to meat and milk in those cases where misuse results in residues in feed items not expected to have residues from approved uses.

Since ruminant and poultry metabolism studies are now to be required in cases where very low or non-detectable residues are present on feed items, the question arises as to what dose level is appropriate. Following FAO's lead, we suggest ≈10 ppm in the diet as the dosing level. This will typically represent 200-1000x the anticipated dietary burden for livestock when trace residues occur in feed items. The radiolabeled material should have sufficient specific activity to enable detection of ≈0.01 ppm (10 ppb) in milk, tissues, and eggs.

As already stated in the Guidelines, the ruminants and/or poultry (depending on feed items involved) should be dosed with radiolabeled material for at least three consecutive days with milk or eggs collected daily. Animals should be sacrificed within 24 hours of the final dose and total radioactivity measured in edible tissues and milk/eggs.

With regard to the degree of characterization of residues in animal (and plant) metabolism studies, a strategy developed by Ciba Geigy may be used as a guide to what effort should be expended (Reference 1). If total activity in a tissue (or crop part) is ≈0.01 ppm (10 ppb) or less, no differentiation of the radioactivity would be required. For activity greater than ≈0.01 ppm the sample should be extracted with organic solvents (perhaps mixed with neutral water). The levels of extractable and non-extractable (NE) activity should then be quantitated to determine the degree of characterization that is needed. If the extractable activity represents ≈0.01 ppm or less in the original sample, it need not be examined further. For extractable activity of ≈0.01-0.05 ppm, the partitioning behavior between aqueous and an organic solvent should be determined followed by chromatographic (TLC, HPLC) analysis of the organosoluble activity. The chromatographic behavior of this activity can be compared to that of the parent pesticide and likely metabolites. When the extractable activity exceeds ≈0.05 ppm, complete characterization should usually be attempted (however, note discussion on highly exaggerated doses below). Identities of metabolites should be confirmed with a second technique, spectroscopic if possible.

With regard to the non-extractable (NE) residues obtained above, further characterization should be attempted when the NE activity in a sample is greater than ≈0.1 ppm or 10% of the total activity in that sample. Attempts should be made to release these residues by acidic or basic hydrolyses and/or enzyme treatments. The degree of characterization needed for the released activity will depend upon its total level in ppm using the figures outlined in the previous paragraph (i.e., ≈0.01, 0.01-0.05, and >0.05 ppm) for extractable residues.

It should be noted that the above ppm "trigger" values are not absolute requirements, but rough guides as to how much characterization is adequate. In the metabolism studies wherein highly exaggerated feeding levels are employed and low activity results in tissues, characterization requirements should be less stringent than when expected dietary burdens lead to significant activity in animal products. For example, if the anticipated dietary burden to livestock is about 0.01 ppm, 10 ppm radio-labeled compound is fed (1000x), and total activities in tissues, milk or eggs are ≤0.1 ppm, minimal characterization of residues should be adequate (unless toxicologists express a special concern with residues at this level). Such situations often arise with early season herbicides having low application rates.

On the other hand, when activities ≥0.1 ppm are observed in animal commodities from ingestion of the pesticide at levels expected on feed items, thorough identification of the residues is generally required. This is likely when pesticides are applied foliarly at high rates through the entire growing season.

Finally, with respect to the need for conventional feeding studies, such data will not be required when no detectable residues are observed in feed items from crop field trials reflecting the proposed use of the pesticide (maximum rate, minimum preharvest interval) unless the metabolism study shows potential for significant bioaccumulation. When trace residues are detected in the field trials, the reviewer should consider the anticipated dietary burdens and the results of the radiolabeled metabolism study when determining whether feeding studies are necessary. In the previously cited example (0.01 ppm dietary burden, 1000x dose leading to <0.1 ppm total activity in meat/milk/eggs), a feeding study would not be necessary as expected residues in animal commodities from ingestion of 0.01 ppm would be on the order of ≈0.1 ppb (assuming linear relation-ship between dose and residues). In this case the metabolism study also serves as a feeding study and tolerances would not be needed for meat, milk, poultry and eggs.

SUMMARY

- **Livestock (ruminant and/or poultry) metabolism studies will be required whenever a pesticide is to be used on a crop having a livestock feed item in Table II of the Residue Chemistry Guidelines.**

•"Trigger values" (ppm radioactivity) are provided as rough guides to the degree of characterization needed in metabolism studies. However, reviewers should take into account how the rate or dose used in the metabolism study compares to that expected from actual use of the pesticide.

•When considering the need for conventional feeding studies in cases where low residues are found in feed items, reviewers should take into account the expected dietary burdens and results of animal metabolism studies. The latter may indicate that residues in animal commodities would be well below detection limits and thus serve as feeding studies. Meat/milk/egg tolerances would not be necessary in such situations.

Reference 1. "STRATEGY FOR DETERMINATION OF EXTENT OF METABOLISM STUDIES AND DEVELOPMENT OF RESIDUE METHODS BASED ON TRIGGER VALUES", 1/27/88, Dr. B. Donzel, Ciba-Geigy.

cc: RF, Petition Review Aids File

ATTACHMENT 4

SUGGESTED STATES FOR CROP FIELD TRIALS

The following lists were prepared in 1983 in response to an IR-4 request as to which states should be included in field trials for representative crops to obtain crop group tolerances. Field trial sites should be representative of the area(s) in which the crop is grown in each state and of the prevailing cultural practices. Arid regions employing furrow irrigation (especially California) should be included for most crops since higher residues are often found under such conditions. Seasonal variation should also be represented.

In cases where a slash appears between states, any one of the states could be used as a site for the residue trial. If a comma appears between states, even if they are in the same region, data for both states is recommended due to the importance of the food crop (e.g., potatoes versus radishes). Residue data for a state/area should consist of a composite sample from several fields. Of course if a state such as PA is recommended for residue trials, substitution of an adjacent state such as NY would be considered acceptable as long as the total number of trials remains the same.

With regard to obtaining tolerances on individual crops (as opposed to crop group tolerances), the lists of states below would suffice in most cases wherein no detectable or low residues are consistently observed in the trials. This would typically be the case for early season, low rate applications of herbicides. It should be noted, however, that for those crops where only 1 or 2 states are shown (e.g., almonds, garlic, radishes) two or more locations should be included in each state.

For those uses which result in significant residues on food or feed portions of crops, the conducting of just one trial in each of the states would usually not be adequate to obtain a tolerance on an individual crop. Either multiple locations in each state or the addition of more states should be considered in such instances. Foliar, high rate applications of fungicides or insecticides throughout the entire growing season would usually fall under this category.

Bulb vegetables (allium)

Garlic	CA
Green onion	TX, CA, AZ/NM
Bulb onion	NY, MI, OR/WA, ID, CO

Roots and tuber vegetables (and their leaves)

Carrots	CA, TX/AZ, MI/WI, WA/OR, NY/NJ, OH, MN
Potato	ID, OR/WA, ND, MN, WI, ME, CA, CO
Radish	FL,CA
Sugarbeets	CA, MN/ND, ID, WA, NE, WY, MI

Roots and tops

Turnip	CA, OR/WA, TX, OH, NJ, IL/IN
Sugarbeets	See Sugarbeets above

Leafy vegetables (non-Brassica)

Lettuce (head and leaf)	CA, FL, TX/AR, NY/NJ, CO, WA
Celery	CA, FL, MI, WA

Spinach	CA, TX/OK, NJ, MD/VA, CO/AR
Brassica vegetables	
Broccoli	CA, TX/AZ, OR
Cabbage	NY, CA, FL, TX, WI, NJ, SC/NC/GA/TN
Mustard Greens	CA, TX/AZ, MI/OH/IN, FL, LA/GA/TN
Legumes (succulent or dried)	
Snap beans	NJ/NY, TN/NC/VA, CA, MI, FL
Green peas	CA, DE, ID, MN, WI, OR/WA
Dry beans	CA, ID, MI, CO, NE, ND
Dry peas	WA/OR, ID
Soybeans	MS/LA, TN, AR, IN/IL, IO/NE, MN, MO
Legumes (foliage)	
Beans	See "Legumes" above
Field peas	See "Legumes" above
Soybeans	See "Legumes" above
Fruiting Vegetables	
Tomato	CA, FL, OH/PA, NJ, IN, MI, SC/TN
Peppers	CA, FL, TX, NC, NJ
Cucurbits	
Cantaloupe	CA, TX/AZ, IN, MI, GA/SC
Summer squash	CA, FL, TX, NJ/MA/NY, OR, GA/SC, MI
Cucumber	CA, FL, TX, MI, NY/NJ, NC/SC, OH
Citrus	
Orange	FL, CA, AZ/TX
Grapefruit	FL, TX, CA
Lemon	CA, AZ
Pome Fruits	
Apples	CA, MI, NY, PA/WV, VA/NC, WA/OR
Pears	CA, MI, NY, WA
Stone fruits	
Peach	CA, GA/SC, MI, NJ/PA, WA
Cherry	CA, OR/WA, MI, UT/MT/ID, NY/PA
Plums	CA, ID, MI, OR/WA
Small fruits and berries	
Blackberry or other *Rubus* spp.	WA, OR
Blueberries	MI, NJ, ME, NC, WA/OR
Strawberry	CA, FL, OR/WA, IN/MI, NY/OH, LA
Cranberry	WI, MA/NJ, OR/WA
Grape	CA, NY, WA, MI, NC

Tree nuts

Almond	CA
English walnut	CA, OR
Pecans	AL/GA/LA/MS, NM/TX/OK

Cereal grains

Wheat	All areas across the country
Sorghum	MO/KS, IL, TX/OK/NM, SD, NE, NC/GA, CO
Rice	AR, CA, LA, TX, MO
Corn (sweet)	FL, CA, NY, TX, OH/PA, MA/NJ, OR/WA/ID, MI/MN/WI, IL
Corn (field)	All areas across the country

Forage, fodder and straw of cereal grains

Corn	See "Corn" above
Wheat	See "Wheat" above
1 other cereal grain crop	See "Rice" above

Grass (including fodder and hay)

Bermuda	All areas across the country
Blue	"
Brome	"
Fescue	"

Non-grass animal feeds (forage, fodder, straw and hay)

Alfalfa	All areas across the country
Clover	"

Herbs and spices

Basil	CA
Chives	CA
Marjoram	CA
Sage	CA
Dill	Southern state, Western state

APPENDIX F: INSTRUCTIONS FOR ELECTRONIC REPORTING

ELECTRONIC SUBMISSION OF PHASE 3 RESPONSES

The agency is currently assessing the advantages of electronic transmission of information required under FIFRA and its amendments. We are conducting research into the many areas where this technology would produce the highest return for both industry and government. We have conducted a pilot project with the chemical industry and determined that there are many other areas we should explore. If your company is interested in electronic reporting, please request an information packet by writing to:

Electronic Reporting
Reregistration Phase 3 Response
Office of Pesticide Programs
P.O. Box 14890
Silver Spring, MD 20910-4890

APPENDIX G: BLANK FORMS FOR PHASE 3 SUBMISSIONS

EPA

United States Environmental Protection Agency
Washington, DC 20460

PHASE 3 IDENTIFICATION OF UNREASONABLE ADVERSE INFORMATION NOT INDICATED ON THE PHASE 3 WORKSHEET

Form Approved

OMB No. 2070-0106

Approval expires 12-92

The public reporting burden for completing this form only is estimated to average approximately 30 minutes per response, including time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information. EPA has accounted for this burden within the total average burden associated with the collection of information under section 4(e)(1)(E). Send comments regarding the burden estimate or any other aspect of this collection of information, including suggesting for reducing this burden, to Chief, Information Policy Branch, PM-223, U.S. Environmental Protection Agency, 401 M St., S.W., Washington, D.C. 20460; and to the Office of Management and Budget, Paperwork Reduction Project (2070-0106), Washington, D.C. 20503.

INSTRUCTIONS

You must use this form to identify each additional item of information on adverse effects that you have not identified on your "Phase 3 Chemical Response Worksheet." For example, you must use this form if you determine that you must identify adverse effects information found in studies that are not listed in the "Phase 3 Chemical Response Worksheet" or if you must identify information found in incident reports.

Please note that this form does not tell you what information constitutes the adverse information that must be identified to EPA. You must consult the guidance on identifying unreasonable adverse effects information that appears in chapter 4 of the "Accelerated Reregistration Phase 3 Technical Guidance" to determine what information must be identified. Once you have determined what information is required, and have determined that you can not identify an item of information on the "Phase 3 Chemical Response Worksheet," you must complete this form to identify that item.

EPA

United States Environmental Protection Agency
Washington, D.C. 20460

PHASE 3 IDENTIFICATION OF UNREASONABLE ADVERSE INFORMATION NOT INDICATED ON THE PHASE 3 WORKSHEET

Form Approved
OMB No. 2070-0106
Approval expires 12-92

Instructions: Please type or print in ink. Please read carefully the attached instructions and supply the information requested on this form. Use additional sheets(s) if necessary.

FILL OUT THIS FORM FOR EVERY SEPARATE ITEM OF ADVERSE EFFECTS INFORMATION.

COMPANY NAME ____________________

COMPANY NUMBER ____________________

CASE NUMBER ____________________

CHEMICAL NUMBER ____________________

CHEMICAL NAME ____________________

1. Does the information pertain to only some of your products? Yes ☐ No ☐

If yes, list the product number(s)

____________________ ____________________

____________________ ____________________

2. Is the source of information a study not identified on the Phase 3 Chemical Response Worksheet, or an incident report or other information source ?

If the source is a study not on your Worksheet, fill out section 3 below.	If the source is an incident report or other source, fill out section 4 below.
3. A. Has the study been submitted to EPA? Yes ☐ MRID Number ____________ Date Submitted ____________ Title ____________ ____________ No ☐ If no, you are required to submit a copy of the study under section 6(a)(2) of FIFRA. B. Attach summary of adverse effects information contained in the study and explain why it may indicate adverse effects.	4. A. Has the information been submitted to EPA? Yes ☐ Date Submitted ____________ How and to whom Submitted ____________ No ☐ If no, you are required to submit a copy of the study under section 6(a)(2) of FIFRA. B. Attach summary of adverse effects information that: 1. Identifies the source of information (e.g. legal proceedings, letter from customer, factory report). 2. Describes the adverse effects and explains why it may indicate adverse effects.

5. **Certification**
I certify that the statements that I have made on this form and all attachments therein are true, accurate, and complete. I acknowledge that any knowingly false or misleading statement may be punishable by fine or imprisonment or both under applicable law.

5 A. Signature of Company's Authorized Representative

____

6. Contact (Typed Name)

7. Phone

EPA

United States Environmental Protection Agency
Washington, DC 20460

PHASE 3 IDENTIFICATION OF UNREASONABLE ADVERSE INFORMATION NOT INDICATED ON THE PHASE 3 WORKSHEET

Form Approved

OMB No. 2070-0106

Approval expires 12-92

The public reporting burden for completing this form only is estimated to average approximately 30 minutes per response, including time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information. EPA has accounted for this burden within the total average burden associated with the collection of information under section 4(e)(1)(E). Send comments regarding the burden estimate or any other aspect of this collection of information, including suggesting for reducing this burden, to Chief, Information Policy Branch, PM-223, U.S. Environmental Protection Agency, 401 M St., S.W., Washington, D.C. 20460; and to the Office of Management and Budget, Paperwork Reduction Project (2070-0106), Washington, D.C. 20503.

INSTRUCTIONS

You must use this form to identify each additional item of information on adverse effects that you have not identified on your "Phase 3 Chemical Response Worksheet." For example, you must use this form if you determine that you must identify adverse effects information found in studies that are not listed in the "Phase 3 Chemical Response Worksheet" or if you must identify information found in incident reports.

Please note that this form does not tell you what information constitutes the adverse information that must be identified to EPA. You must consult the guidance on identifying unreasonable adverse effects information that appears in chapter 4 of the "Accelerated Reregistration Phase 3 Technical Guidance" to determine what information must be identified. Once you have determined what information is required, and have determined that you can not identify an item of information on the "Phase 3 Chemical Response Worksheet," you must complete this form to identify that item.

EPA

United States Environmental Protection Agency
Washington, D.C. 20460

PHASE 3 IDENTIFICATION OF UNREASONABLE ADVERSE INFORMATION NOT INDICATED ON THE PHASE 3 WORKSHEET

Form Approved
OMB No. 2070-0106
Approval expires 12-92

Instructions: Please type or print in ink Please read carefully the attached instructions and supply the information requested on this form. Use additional sheets(s) if necessary.

FILL OUT THIS FORM FOR EVERY SEPARATE ITEM OF ADVERSE EFFECTS INFORMATION.

COMPANY NAME ______________________

COMPANY NUMBER ______________________

CASE NUMBER ______________________

CHEMICAL NUMBER ______________________

CHEMICAL NAME ______________________

1. Does the information pertain to only some of your products? Yes ☐ No ☐

   If yes, list the product number(s)

   ______________________ ______________________

   ______________________ ______________________

2. Is the source of information a study not identified on the Phase 3 Chemical Response Worksheet, or an incident report or other information source ?

If the source is a study not on your Worksheet, fill out section 3 below.	If the source is an incident report or other source, fill out section 4 below.

3. A. Has the study been submitted to EPA?

   Yes ☐ MRID Number ______________
   Date Submitted ______________
   Title ______________
   ____

   No ☐ If no, you are required to submit a copy of the study under section 6(a)(2) of FIFRA.

   B. Attach summary of adverse effects information contained in the study and explain why it may indicate adverse effects.

4. A. Has the information been submitted to EPA?

   Yes ☐ Date Submitted ______________
   How and to whom Submitted ______________

   No ☐ If no, you are required to submit a copy of the study under section 6(a)(2) of FIFRA.

   B. Attach summary of adverse effects information that:

   1. Identifies the source of information (e.g. legal proceedings, letter from customer, factory report).
   2. Describes the adverse effects and explains why it may indicate adverse effects.

5. Certification
   I certify that the statements that I have made on this form and all attachments therein are true, accurate, and complete. I acknowledge that any knowingly false or misleading statement may be punishable by fine or imprisonment or both under applicable law.

5 A. Signature of Company's Authorized Representative

____

6. Contact (Typed Name)

7. Phone

APPENDIX H: ADDITIONAL GUIDANCE ON RAW DATA

EPA has developed the following lists to provide registrants with additional guidance on how to determine whether they have access to the raw data that support the studies they are relying on for reregistration.

RECORDS TO BE MAINTAINED FOR SUBDIVISION D

The following listing covers studies for submission under Subdivision D. Records to be maintained include but are not necessarily limited to the following:

*1. Name and address of testing facility and Principal Investigator

*2. Name and address of registrant / test sponsor

*3. Test substance type, source, strength, identification and purity (batch/lot numbers), and, procedures used to manufacture or synthesize the test substance

*4. Analytical test data for all components

*5. Analytical methods

*6. Documentation of certified limit determinations

*7. Test method identification (reference) or description

*8. Analytical raw data for test

*9. Signed final report

10. Test substance receipt and distribution

11. List of participants and their training and experience

12. Inspection / calibration / standardization of equipment

13. Standard Operating Procedures

14. Correspondence

* Minimum requirements

RECORDS TO BE MAINTAINED FOR SUBDIVISION E

The following listing covers studies for submission under Subdivision E in general, including laboratory, simulated or actual field testings as appropriate. Records to be maintained include but are not necessarily limited to the following:

*1. Name and address of testing facility and Principal Investigator

*2. Name and address of registrant / test sponsor

*3. Test substance

- identification, strength, purity and composition
- storage requirements
- solubility
- storage stability
- preparation of dosages
- application procedures
- amount administered / dosage level
- stability in mixture
- solubility in mixture

*4. Description of test site

- location
- layout (terrain, soil type)

*5. Methodology/ standard or EPA approved procedures

*6. Environmental condition

- water depth, pH, temperature, relative humidity, salinity, dissolved oxygen, etc.

*7. Census of existing population

- mammalian, avian, amphibians, insects, etc.
- vegetation, soil types, etc.
- mobile species (transients): fish, wildlife, humans, etc.

*8. Set up of study

- number of animals
- size, age, sex

* Minimum requirements

SUBDIVISION E CONTINUED

*9. Experimental data

- weights
- mortality
- observations/behavior

*10. Sample collection data

*11. Activities around field / test site and unforeseen circumstances that may affect test results

*12. Signed final report

13. Test substance receipt and distribution

14. Animal receipt, randomization, distribution

15. Animal health records prior to the start of the study

16. List of participants and their training and experience

17. Inspection / calibration / standardization of equipment

18. Standard Operating Procedures

19. Correspondence

20. Housing conditions: number per container, lighting, etc.

21. Method of counting

* Minimum requirements

RECORDS TO BE MAINTAINED FOR SUBDIVISION F

The following listing covers studies for submission under Subdivision F in general, including mammalian toxicity and mutagenicity testings as appropriate. Records to be maintained include but are not necessarily limited to the following:

*1. Name and address of testing facility and Principal Investigator

*2. Name and address of registrant / test sponsor

*3. Test substance

- identification, strength, purity and composition
- solubility
- storage requirements
- storage stability / viability of the cell cultures
- preparation of dosages
- amount administered / dosage level
- application procedures
- stability in mixture
- solubility in mixture

*4. Methodology / standard or EPA approved procedures

*5. Environmental condition

*6. Set up of study

- number of animals
- size, age, sex
- cell culture (test system)
- type of media used

*7. Experimental data

- weights
- mortality / viability of cells
- observations / behavior
- feed consumption
- analytical chemistry
    - homogeneity of dosage preparation
    - stability of dosage preparation
    - dosage analyses
- genotoxic effects
- clinical pathology

* Minimum requirements

SUBDIVISION F CONTINUED

- necropsy
- wet tissues
- histopathology
- tissue blocks / slides

*8. Unforeseen circumstances that may have an effect on the test results

*9. Signed final report

10. Test substance receipt and distribution

11. Animal receipt, randomization, distribution

12. Animal health records prior to the start of the study

13. List of participants and their training and experience

14. Inspection / calibration / standardization of equipment

15. Standard Operating Procedures

16. Correspondence

* Minimum requirements

RECORDS TO BE MAINTAINED FOR SUBDIVISION J

This general listing covers studies for submission under Subdivision J, including greenhouse or field tests as appropriate. Records to be maintained include but are not limited to the following:

*1. Name and address of testing facility and Principal Investigator

*2. Name and address of registrant / test sponsor

*3. Test substance

- chemical name, percent active ingredient and formulation, amounts of impurities, inerts, solvents, etc.
- water solubility
- vapor pressure
- solvents in controls

*4. Date of test initiation and termination

*5. Test organism

- history and source
- identification of test species (family, genus, species, cultivar / variety)

*6. Test design

- observation period
- criteria used to measure effects
- test solution, preparation method
- water source and description
- test vessel size, type
- dose rates in ppm and #ai/A, number of treatment levels
- type and number of controls
- number of replicates
- physical and chemical properties (pH, % organic matter) of substrate / media
- protocols used for growth measurements and rating systems
- test organism and control group assignment method
- size, location, and air flow of growth chamber, greenhouse, field plot
- environmental conditions: thermoperiod; relative humidity; lighting regime - intensity, quality, photoperiod; watering regime - frequency, amount
- cultural practices

*7. Statistical analysis method and results

* Minimum requirements

SUBDIVISION J CONTINUED

*8. Discussion and results - signed final report with:
  - EC25 and EC50 values in ppm and #ai/A with 95% confidence limits
  - Test vs control growth measurements from which calculations are made (cells/ml/vessel, plants/vessel, etc.)
  - No observed effect level
  - Phytoxicity symptoms observed

*9. Standard Operating Procedures, EPA protocols used

*10. Deviations from EPA guidelines and rationale. Report problems encountered during the study and the effect they may have had on the study outcome.

*11. Inspection / calibration / standardization of equipment

*12. Correspondence

13. Test substance receipt and distribution

* Minimum requirements

RECORDS TO BE MAINTAINED FOR SUBDIVISION K

The following listing covers studies for submission under Subdivision K. Records to be maintained include but are not necessarily limited to the following:

*1. Name and address of testing facility and Principal Investigator

*2. Name and address of registrant / test sponsor

*3. Test substance type, source, identification (batch or lot numbers) and strength

*4. Identification of facility and test plots

*5. Informed consent documentation for testing on humans, if appropriate

*6. Test system identification, source and preparation

*7. Test substance preparations: how and when test substance was prepared (diluted)

*8. Test substance applications: how and when applied and amount applied

*9. Sampling technique, identification, preservation and transfer to laboratory

*10. All analytical raw data, including quality control determinations

*11. Stability data, if appropriate, for test substance / metabolites: Frozen, if analyses are more than one week after sampling; not frozen for analyses one day after sampling.

*12. Signed final report

13. Test substance receipt and distribution

14. List of participants and their training and experience

15. Inspection / calibration / standardization of equipment

16. Standard Operating Procedures

17. Correspondence

* Minimum requirements

RECORDS TO BE MAINTAINED FOR SUBDIVISION L

The following listing covers studies for submission under Subdivision L in general, including laboratory and simulated or actual field tests as appropriate. Records to be maintained include but are not necessarily limited to the following:

*1. Test sponsor (name of study owner)

*2. Name and address of testing facility

*3. Name of principal investigator

*4. Location where study was conducted

*5. Test dates

*6. Location of raw data and final report

*7. Test substance:

- common and trade name
- chemical name and composition
- percent active ingredient
- source, lot number, or code

*8. Preparation of test material:

- vehicle used to dissolve or dilute test substance
- preparation methods
- total amount of test material used

*9. Test insects:

- source of supply of test bees
- methods used to obtain test bees from colonies
- history of test bees
- health status of test bees
- age of bees at test initiation

*10. Test design:

- Size and composition of test cages
- Procedures used to prepare toxicant solution
- Criteria used to determine effects
- Amount of test material per bee or per acre

* Minimum requirements

SUBDIVISION L CONTINUED

- Method of administration / application
- Name of treated crop
- Weather conditions during and after application
- Method used to harvest treated foliage
- Amount of treated foliage per cage
- Rationale for selection of method, route, or frequency of application, if different from that recommended in Subdivision L
- Method used in assigning bees to test and control groups
- Number of treated levels
- Number of replicates used
- Number of bees per treatment level and control
- Method used to determine treatment levels
- Number of bees per cage
- Number and types of controls
- Environmental conditions (ambient temperature, humidity, weather conditions)
- Source and availability of food and water
- Length of total observation period
- Frequency and duration of observations
- Length of study

*11 Statistical analysis (method or references)

*12 Reported results:

- LD50 in micrograms per bee, with 95% confidence limits
- No-observed-effect level
- Slope of the dose-response line, if the method provides a slope
- Percent mortality of test bees at each treatment level and time interval
- Raw mortality data
- Detailed description of all observed toxic effects
- Description of any deviation from recommended protocol

* Minimum requirements

RECORDS TO BE MAINTAINED FOR SUBDIVISION M

The following listing covers studies for submission under Subdivision M for microbial pest control agents, including laboratory, simulated or actual field testings as appropriate. Biochemical pest control agents are tested using protocol similar to conventional chemical pesticides and, for biochemical pesticides, the record maintenance requirements for conventional chemical testing should be followed. Records to be maintained for microbial pesticides include but are not necessarily limited to the following:

*1. Name and address of testing facility and Principal Investigator

*2. Name and address of registrant / test sponsor

*3. Test substance

   a. All criteria used to arrive at characterization, including taxonomic placement of the microorganism.

   b. Information on the developmental biology and reproduction cycle of the microorganisms.†

   c. Confinement measures of the microorganisms

   d. Known pathogen features of the organism that may vary with the environment.†

   e. Units of active microbial ingredient in dosing / test material.

   f. Expected limits of detection of the microorganism.

   g. Maintenance of test substance.

   h. Preparation of test material for dosing.

   i. Characterization of any microbial contamination

   j. Source for each cell line / parental material

   k. Survival of the microorganisms over the course of the test

   l. Storage requirements (temperature)

   m. Application procedures

   n. Stability of test substance in mixtures

† Required only for field studies

* Minimum requirements

SUBDIVISION M CONTINUED

*4. Description and location of test site.**

*5. Methodology / standard or EPA approved procedures

   a. Description of test protocols used

   b. Analytical methods for culturing, isolation, identifying, and assuring the purity of the microbial cultures used in the experiments.

*6. Environmental or testing conditions: water depth, pH, temperature, relative humidity, etc.

*7. Study design

   a. Size, sex, age, number, etc. of animals

   b. Acclimation of test system, housing

   c. Animal receipt, randomization, distribution

   d. Animal health records prior to the start of the study.

*8. Census of existing population†

   a. Mammalian, avian, amphibians, insects, etc.

   b. Vegetation, soil types, etc.

   c. Mobile species (transients): fish, wildlife, humans)

*9. Sample collection data†

*10. Unforeseen circumstances and activities around field / test site that may have an effect on the test results†

*11. Signed final report

*12. Test substance receipt and distribution.

† Required only for field tests

* Minimum requirements

RECORDS TO BE MAINTAINED FOR SUBDIVISION N

The following listing covers studies for submission under Subdivision N. Records to be maintained include but are not necessarily limited to the following:

*1. Name and address of testing facility and Principal Investigator

*2. Name and address of registrant / test sponsor

*3. Test substance type, source, identification (batch or lot number) and purity

*4. Test system source, identification and preparation (also processing, if appropriate)

*5 Test locations
  - Geographical location of facilities
  - Specific locations of treatment plots

*6. Application of test substance to test system
  - How and when test substance was prepared
  - How and when test substance was applied
  - Amount applied
  - Meteorological conditions at application
  - Equipment conditions at application

*7. Test system sampling and sample identification

*8. Sample preservation and shipment to laboratory

*9. All analytical data with quality control determinations

*10. Stability data, for test substance and / or metabolites: frozen, if analyses are more than one week after sampling; not frozen for analyses within one day after sampling.

*11. Signed final report

12. Test substance receipt and distribution

13. List of participants and their training and experience

*14. Inspection / calibration / standardization of equipment

*15. Standard Operating Procedures

*16. Correspondence

* Minimum requirements

RECORDS TO BE MAINTAINED FOR SUBDIVISION O

The following listing covers studies for submission under Subdivision O. Records to be maintained include but are not necessarily limited to the following:

*1. Name and address of testing facility and Principal Investigator

*2. Name and address of registrant / test sponsor

*3. Test substance type, source, identification (batch or lot number) and strength

*4. Test plot locations
  - General geographical location of facility
  - Specific locations of treatment and controls within facility
  - Weather conditions at the test plot
  - History of any previous pesticide use on the test plot

*5. Test system, identification and preparation (also processing, if appropriate)

*6. Test substance preparations and applications
  - How and when test substance was prepared (diluted)
  - How and when test substance was applied
  - Amount of test substance applied

*7. Test system sampling preparation, including procedures for subsampling (when and how) and sample identification

*8. Sample preservation and shipment to laboratory

*9. All analytical raw data, including quality control determinations

*10. Stability data, if appropriate, for test substance and / or metabolites: frozen, if analyses are more than one week after sampling; not frozen for analyses within one day after sampling.

*11. Signed final report

12. Test substance receipt and distribution

13. List of participants and their training and experience

*14. Inspection / calibration / standardization of equipment

15. Standard Operating Procedures

16. Correspondence

* Minimum requirements

RECORDS TO BE MAINTAINED FOR SUBDIVISION R

The following listing covers studies for submission under Subdivision R. Records to be maintained include but are not necessarily limited to the following:

*1. Name and address of testing facility and Principal Investigator

*2. Name and address of registrant / test sponsor

*3. Test substance type, source, identification (batch or lot number) and purity

*4. Test system source and preparation

*5. Test locations

- Geographical location of facilities
- Specific locations of treatment plots

*6. Application of test substance to test system

- How test substance was prepared
- How and when test substance was applied
- Quantity applied
- Meteorological conditions at application
- Equipment conditions at application

*7. Test system sampling and sample identification

*8. Sample preservation and shipment to laboratory

*9. All analytical data with quality control determinations

*10. Stability data for test substance until analyzed

*11. Signed final report

12. Test substance receipt and distribution

13. List of participants and their training and experience

*14. Inspection / calibration / standardization of equipment

*15. Standard Operating Procedures / Protocols

*16. Correspondence

* Minimum requirements

RECORDS TO BE MAINTAINED FOR SUBDIVISION U

The following listing covers studies for submission under Subdivision U. Records to be maintained include but are not necessarily limited to the following:

*1. Name and address of testing facility and Principal Investigator

*2. Name and address of registrant / test sponsor

*3. Test substance type, source, identification (batch or lot number) and strength

*4. Identification of facility and test plots

*5. Informed consent documentation for testing on humans

*6. Test system (dosimeter) preparation and locations

*7. Test substance preparations and applications

  - How and when test substance was prepared (diluted)
  - How and when test substance was applied
  - Amount applied

*8. Sample identification, preservation and transfer to laboratory

*9. All analytical raw data, including quality control determinations

*10. Stability data, if appropriate, for test substance if analyses are more than one week after sampling

*11. Signed final report

12. Test substance receipt and distribution

13. List of participants and their training and experience

14. Inspection / calibration / standardization of equipment

15. Standard Operating Procedures

16. Correspondence

* Minimum requirements

APPENDIX I: GUIDELINES FOR IDENTIFYING INFORMATION CONCERNING UNREASONABLE ADVERSE EFFECTS PURSUANT TO FIFRA SECTION 4(e)(1)(E)

GUIDELINES FOR IDENTIFYING INFORMATION CONCERNING UNREASONABLE ADVERSE EFFECTS PURSUANT TO FIFRA SECTION 4(e)(1)(E)

1. What the law requires of registrants.

Section 6 (a)(2) of the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) states: "If at any time after the registration of a pesticide the registrant has additional factual information regarding unreasonable adverse effects on the environment of the pesticide, he shall submit such information to the Administrator."

Section 4(e)(1)(E) of FIFRA requires a registrant seeking reregistration to submit "an identification of the data that are required to be submitted to the Administrator under Section 6(a)(2) indicating an adverse effect of the pesticide."

Section 4(e)(4) of FIFRA requires the Administrator to issue guidelines to be followed by registrants in identifying adverse information. Compliance with these guidelines will satisfy a registrant's obligations to submit data pursuant to section 4(e)(1)(E).

2. Section 4(e)(1)(E) Submission.

Who Must Submit Information. Each registrant who submitted a Phase II response indicating his intent to reregister his product(s) and who agreed that he is responsible for generating data is required to identify and submit adverse effects information required by this guidance document. This includes only registrants who submitted Parts A and B in their Phase II response.

Definitions.
"Pesticide" means all active ingredients, inert ingredients, impurities, metabolites, and degradates of the pesticide product for which reregistration is sought.

"Formal Review" means Special Review, Rebuttable Presumption Against Registration (RPAR), FIFRA section 6(c) proceeding, or FIFRA section 6(b) cancellation proceeding.

"Established Levels" means tolerances, food additive regulations, action levels, or other limitations on residues imposed by law, regulation or other authority.

"Water Reference Level" means the Maximum Contaminant Level (MCL), if one has been established by EPA, or if it has not, the most recent draft or final long term Health Advisory Level for the most sensitive subpopulation, such as children. If EPA has published no such levels, the water reference level is any amount of pesticide detected.

What information must be identified and submitted.
Information must be identified and submitted if the registrant, or any officer, employee, or agent of the registrant possesses or knows of the information.

Information must be identified and submitted if it meets one or more of paragraphs 2 through 10.

Interim test results, raw test data, and other information from an ongoing or uncompleted study must be identified and submitted if:

adverse effects which would be reportable in a completed study have been observed, and the registrant has been advised, or a reasonable person would conclude, that the effects may be attributable to exposure to the substance tested; or

the pesticide has been detected in food, feed, and water in amounts that would require the information to be reported under paragraph 6, if the study were complete.

Opinion Information. Opinion information must be identified and submitted if it consists of opinion(s) or conclusion(s) expressed by a person:

Who was employed or retained (directly or indirectly) by the registrant; or

From whom the registrant requested the opinion(s) or conclusion(s) in question; or

Who by virtue of his knowledge, skill, experience, training, or education could be considered to be an expert with regard to the matter on which he rendered the opinion.

Clearly erroneous information. Information need not be submitted if prior to the date the Phase III submission is due to be filed with EPA:

The registrant discovers that any analysis, conclusion, or opinion was predicated on data that were erroneously generated, recorded, or transmitted, or on computational errors; and

Every author of each such analysis, conclusion, or opinion has acknowledged in writing that the analysis, conclusion, or opinion was improper because of the use of the erroneous data, and has corrected the original analysis, conclusion, or opinion accordingly; and

As a result of the correction, the information is no longer required to be reported under FIFRA section 6(a)(2).

3. Data that must be submitted: toxicological and ecological studies.

The results of a completed study of the toxicity to any human or other non-target organism of a pesticide must be submitted if the substance tested had a toxic or adverse effect which has not been previously reported to EPA in a study which meets the requirements of 40 CFR Part 160, or which in comparison to such a previously submitted valid study shows a toxic or adverse effect:

- in a different organ or tissue of the test organism; or
- at a lower dosage, or after a shorter exposure period, or after a shorter latency period; or
- at a higher incidence or frequency; or
- in a different species, strain, sex, or generation of test organism; or
- by a different route or medium of exposure; or
- through a different pharmacokinetic, metabolic, or biological mechanism; or
- of greater severity.

However, a study that demonstrates any toxic or adverse effect of a pesticide must be identified and submitted if the pesticide is or has been the subject of a Formal Review.

4. Data that must be submitted: Human epidemiological studies and residue monitoring data.

Information which concerns any study (or portion thereof) upon which a reasonable person would conclude that a positive correlation or association may exist between exposure to a pesticide and adverse effects in humans, or residues of these pesticides in human tissue or body fluid, must be submitted regardless of whether or not the registrant considers any observed correlation or association to be significant.

5. Data that must be submitted: Efficacy studies.

Information which concerns any study of the efficacy of a pesticide must be submitted if:

- The information demonstrates that the pesticide may not perform in accordance with any claim by the registrant regarding uses intended for control of organisms which may pose a hazard to human health; or
- The information shows any deficiency or reduction in claimed efficacy of the pesticide, if the pesticide is, or in the past has been, the subject of a Formal Review.

6. Data that must be submitted: Studies of pesticides on food or feed, or in water.

Food and Feed: Information must be submitted if it is from a study which may show that the pesticide is present on food or feed at a level in excess of established levels, except that information on excess residues resulting solely from studies conducted under authority of FIFRA section 5 need not be submitted.

Water: Information must be submitted if it is from a study which may show that the pesticide:

- Is present in waters of the United States, (as defined at 40 CFR 122.2, except paragraph (d) of section 122.2) above the "Water Reference Level", as defined in these guidelines.
- Is present is groundwater above the "Water Reference Level", as defined in these guidelines.
- Is present in finished drinking water above the "Water Reference Level", as defined in these guidelines.

However, information need not be submitted regarding the presence of the pesticide if it is registered for use in finished drinking water or surface water and the amounts do not exceed those amounts reported by a registrant, in his application for registration, as resulting from legal applications of pesticides to water.

7. New metabolites, degradates, contaminants.

Information which shows the existence of any substance which appears to be a metabolite, degradate, or contaminant of a pesticide must be submitted if:

- The substance may occur under conditions of use of the pesticide, and
- The existence of the substance or the association of the substance with the pesticide has not previously been reported to EPA, and
- The registrant has concluded, or has been advised that the substance is of toxicological or ecological concern, or

- The registrant has concluded, or has been advised that the substance, or analogous chemicals, may degrade less than 10% in 30 days, or
- A reasonable person would conclude that the substance may be of toxicological or ecological concern based on:
    - the physical chemical properties of the new substance; and/or
    - data regarding analogous chemicals; and/or
    - data regarding chemical reactivity of the new substance and analogous substances; and/or
    - data on the new substance.

8. Data that must be submitted: Toxic or adverse effect incident reports.

Single incidents: Information regarding a single toxic or adverse effect incident must be submitted if:

- The registrant has been informed that a person or other non-target organism suffered an adverse effect; and
- The registrant has been informed that the affected person or other non-target organism may have been exposed to the pesticide, or to one or more of its ingredients; and
- Either :
    - The registrant has received sufficient information to investigate the reported incident and has failed to conduct a reasonable investigation prior to the date of the Phase III submission; or
    - The registrant has concluded or has been advised that there is a causal relationship between the adverse effect and exposure to its pesticide.

Exceptions: Information regarding a single toxic or adverse effect need not be submitted if:

- It concerns minor irritation of human skin or the eye when the label provides adequate notice of such a hazard; or
- It concerns non-lethal adverse effects to non-target plants which were at the use site at the time the pesticide was applied.
- It concerns adverse effects to non-target plants which the registrant can conclusively demonstrate were due to misuse of the pesticide.

Series of incidents. Information concerning any series or pattern of similar incidents attributable to one of the registrant's products must be reported unless the causal relationship between the adverse effect and exposure to the registrant's pesticide has been conclusively disproved. For purposes of this section a series or pattern of incidents means 3 or more similar occurrences within the 5 years preceding submission of information under these guidelines, except, for incidents of adverse effects to humans, a series or pattern of incidents means 3 or more similar occurrences within the 10 years immediately preceding submission under these guidelines. Notwithstanding the above, information pertaining solely to non-lethal adverse effects to non-target plants at the use-site at the time the pesticide was applied need not be submitted if adequate warnings of the effect appear on the label of the registrant's product.

9. Failure of performance incident reports.

Immediate hazard to human health. Information must be submitted which concerns an incident in which:

- The registrant has been informed that a pesticide product did not perform as claimed against target organisms; and
- The registrant has received sufficient information to conduct an investigation of the incident and prior to the date of the Phase III submission, has not disproved the failure of performance; and
- The failure of the pesticide to perform as claimed involved the use against organisms which, unless controlled, may pose an immediate hazard to human health.

Risk to human health. Information must be submitted which concerns a series or pattern of 3 or more similar incidents in which:

  - The registrant has been informed that a pesticide product did not perform as claimed against target organisms; and
  - The registrant has received sufficient information to conduct an investigation of 3 or more incidents prior to the date of the Phase III submission, and has not proved that the failures of performance occurred less than 3 times; and
  - The failures of the pesticide to perform as claimed involved the use against organisms which, unless controlled, may pose a risk to human health, and
  - The three or more incidents occurred within the 10 years preceding submission of information under these guidelines.

Products subject to Formal Review. Information must be submitted which concerns a series or pattern of three or more individual incidents as to which:

- The registrant has been informed of three of more similar type of failures to perform as claimed against target organisms; and
- For at least three individual incidents the registrant has received sufficient information to conduct an investigation and, prior to the date of the Phase III submission, has failed to establish that the reported failure of performance did not occur; and
- The failure of the pesticide to perform as claimed involved any use of a pesticide, if the pesticide is, or in the past has been the subject of a Formal Review; and
- The three or more incidents occurred within the 10 years preceding submission of information under these guidelines.

10. Incidents of pesticides on food or feed, or in water.

Food and feed. Information must be submitted if it relates to an incident which shows that the pesticide is present on food or feed at a level in excess of established levels.

Water. Information must be submitted if it is from an incident which shows that the pesticide:

- Is present in waters of the United States (as defined at 40 CFR 122.2, except paragraph (d) of section 122.2) above the Water Reference Level, as defined in these guidelines.
- Is present in groundwater above the "Water Reference Level", as defined in these guidelines.
- Is present in finished drinking water above the "Water Reference Level", as defined in these guidelines.

However, information need not be submitted regarding the presence of the pesticide if it is registered for use in finished drinking water or surface water and the amounts do not exceed those amounts reported by a registrant, in his application for registration, as resulting from legal applications of pesticides to water.

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11. Reporting of other information.

If the registrant knows of information regarding unreasonable adverse effects on the environment of the pesticide, he shall submit such information to the Administrator.

12. Note.

EPA reserves the right to request additional information regarding exposure or other information during reregistration phase IV. Although EPA will use the above standards as thresholds for adverse effects under FIFRA section 4(e)(1), during phase IV such information as exceedances of State Water Quality Standards, monitoring data, or other data in registrants' possession may be required.